약학석사학위논문

Chemical Constituents from *Cudrania tricuspidata*

꾸지뽕나무의 화학 성분

2018년 2월

서울대학교 대학원
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최 영 헌

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이 논문을 약학석사 학위논문으로 제출함

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최영헌의 약학석사 학위논문을 인준함

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Abstract

Cudrania tricuspidata Bureau, belonging to Moraceae family, is mainly distributed in Korea, Japan and China. Leaves of *C. tricuspidata* have been used for eczema, mumps, tuberculosis as a traditional medicine. Phytochemical studies revealed that major constituents of this plant are various types of flavonoids xanthones.

The leaves and twigs of *C. tricuspidata* were extracted with 100% methanol. The extract was suspended in H_2O and the subsequently fractionated with *n*-hexane, $CHCl_3$, EtOAc and *n*-BuOH. Thirty compounds were isolated from EtOAC, *n*-BuOH by various chromatographic techniques. Structure of compounds was elucidated based on NMR, MASS and FT-IR spectroscopic data. Compounds were identified as 4'-glucopyranosyloxybenzyl-4-*O*-*β*-D-glucopyranosyloxy-3,5-dimethoxybenzoate (**1**), Bis [4-*O*-*β*-D-glucopyranosyloxy)benzyl] 3-hydroxy-3-methylglutarate (**2**), Gastrodin (**3**), *p*-hydroxybenzaldehyde-4-*O*-*β*-D-glucopyranoside (**4**), 3,4,5-trimethoxy phenyl-1-*O*-*β*-D-glucopyranoside (**5**), Cudrabibenzyl A (**6**), (6*S*, 9*R*)-Roseoside (**7**), 3-*O*-caffeoyl-2-*C*-methyl-D-erythrono-1,4-lactone (**8**), Chlorogenic acid (**9**) Umbelliferone (**10**), Skimmin (**11**), Esculin (**12**), *C*-veratroylglycol (**13**), 2,3-dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)propan-1-one (**14**), 4-hydroxy benzoic acid (**15**), Methyl-4-hydroxy benzoate (**16**), Quercetin (**17**), Quercetin-3-*O*-*β*-D-glucopyranoside (**18**), Quercetin-7-*O*-*β*-D-glucopyranoside (**19**), Kaempferol-7-*O*-*β*-D-glucopyranoside (**20**), Nicotiflorin (**21**), Aromadendrin (**22**), Aromadendrin-7-*O*-*β*-D-glucopyranoside (**23**), Gericudranin E (**24**), Taxifolin (**25**), Dihydromorin (**26**),

Orobol (**27**), Orobol-7-*O*-*β*-D-glucopyranoside (**28**), Ambocin (**29**), 5-methoxy-8-glucopyranosyl-genistein (**30)**. Compounds **1**-**5** were phenolic type, compound **6** was stilbenoid type, compound **7** was megastigmane derivative, compounds **8**-**9** were caffeoyl derivatives**,** compounds **10**-**12** were coumarin type, compounds **13**-**14** were phenylpropanoid type, compounds **15**-**16** were benzoic acid derivatives, compounds **17**-**30** were flavonoid type. Among them, compounds **1** and **2** were newly reported in nature. Compounds **3**, **4**, **5**, **13**, **14**, **15**, **16**, **29** were newly reported from Moraceae family. Compounds **7**, **11**, **12** were newly reported from *Cudrania* genus.

Keyword : *Cudrania tricupidata*, Moraceae, flavonoid

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List of Abbreviations

ACN : acetonitrile

$[\alpha]_D$: specific rotation

br s : broad singlet

n-BuOH : *n*-buthanol

CC : column chromatography

$CHCl_3$: chloroform

COSY : correlation spectroscopy

d : doublet

dd : doublet of doublet

DMSO : dimethyl sulfoxide

ESI : electrospray ionization

EtOAc : ethyl acetate

fr : fraction

FT-IR : Fourier-transform infrared spectroscopy

HMBC : heteronuclear multiple bond correlation

HPLC : high performance liquid chromatography

HR : high resolution

HSQC : heteronuclear single quantum coherence

Hz : hertz

m : multiplet

MeOH (M) : methanol

MPLC : medium pressure liquid chromatography

MS : mass spectrometry

NMR : nuclear magnetic resonance

Q-TOF : quadrupole-time of flight

RP : reverse phase

s : singlet

UV : ultraviolet absorption spectroscopy

Chapter1. Introduction

Cudrania tricuspidata Bureau, a deciduous tree with thorns, is mainly distributed in Korea, Japan and China (East Asia). Leaves of *C. tricuspidata* have an egg-shape or they are divided into three parts. Their length is 6-10cm and their width is 3-6cm. They have been used for eczema, mumps, tuberculosis as traditional medicine. (Medicianl plants of Korea. 2004)

A number of studies have revealed the chemical consitituents from *C. tricuspidata*. Two major classes of constituents from *C. tricuspidata* have been considered to be flavonoids and xanthones (Xin et al. 2017). Some flavonoids from fruits of *C. tricuspidata* were prenylated or benzylated (Han et al. 2009). Several isoflavonoid from leaves of this plant were prenylated (Tuan Anh et al. 2017). Also, some xanthones from roots of this plant were prenylated (Kwon et al. 2014).

Pharmacological studies reported that leaves of *C. tricuspidata* including abundant flavonoids, had antioxidant activity and xanthine oxidase inhibitory activity (Song et al. 2017). Leaves of *C. tricupidata* inhibited NO production in RAW 264.7 cell (Tuan Anh et al. 2017) and they also had antiobesity and antidiabetes effects through PTP1B inhibitory activity, (Kim et al. 2016) α-glucosidase inhibitory activity (Son et al, 2013) and pancreatic lipase inhibitory activity (Kim et al. 2012).

Pharmacological study reported that twigs of *C. tricuspidata* including several

flavanol glycosides, showed strong tyrosinase inhibitiory activity (Zheng et al. 2013) and they also had a hypopigment activity against melanogenesis through tyrosinase inhibitiory activity. (Hu et al. 2013)

The study of chemical constituents from leaves or twigs of *C. tricuspidata* has been rarely reported, compared to one of chemical constituents from fruits or roots of *C. tricuspidata*. Thus, the purpose of this study was to isolate the chemical constituents from leaves and twigs of *C. tricuspidata* and to elucidate their structure.

Chapter2. Experimental Section

2.1. Material

2.1.1. Plant material

The leaves and twigs of *C. tricuspidata* were collected from the Herbarium in the medical plant garden, Seoul National University, in May 2015.

2.1.2. Reagents

Diaion HP-20 (Mitsubishi Chemical Corporation, Japan), Sephadex LH-20 (25–100 μm; Pharmacia, USA) and Kiesegel 60 silica gel (40-63 μm, 230-400 mesh, Art. 9385; Merck, Germany) were used for column chromatography (CC). Pre-coated Kiesegel 60 silica gel F_{254} plates (Art. 5715; Merck, Germany) were used for Thin-Layer Chromatography (TLC). HPLC grade solvents were purchased from Fisher Scientific Korea Ltd. (Korea). First grade solvents for extraction and for isolation procedures, were purchased from Daejung Chemical & Metals Co. Ltd. (Korea). $CDCl_3$, CD_3OD and DMSO-d_6 (Cambridge Isotope Laboratories, Inc. USA) were used for NMR solvents. L-cysteine methyl ester hydrochloride and *o*-tolylisothiocyanate were purchased from Tokyo Chemical Industry (Japan).

2.1.3. Equipments

Analytical balance : Mettler ML 204, Switzerland

Analytical RP-HPLC system : Waters 2695 alliance system with a 996 Photodiode Array detector, USA

UV : Chirascan plus Circular Dichroism spectrometer, UK

Evaporator : EYELA R-1000, Japan

Freeze-dryer : DURA-DRY, Fts system Inc., USA

FT-IR : Jasco FT/IR-4200 spectrophotometer, Japan

HR-ESI-QTOF-MS : Waters Xevo G2 qTOF mass spectrometer, UK

MassLynx SCN 855 software for data acquisition

NMR : Jeol JMN-LA 300 Spectrometer, Japan

Bruker AVANCE 300 Spectrometer, Germany

Bruker GPX 400 Spectrometer, Germany

Bruker AVANCE 500 Spectrometer, Germany

MPLC : Combiflash companion, Isco, USA

MPLC column : RediSep 120 g silica flash column, Isco, USA

Polarimeter : Jasco P- 2000 digital polarimeter, Japan

UV lamp : VL-4.LC, 365/254, Vilber Lourmat, France

HPLC for isolation : Gilson HPLC equipped with Gilson 321 pump and UV.VIS 151 detector, USA

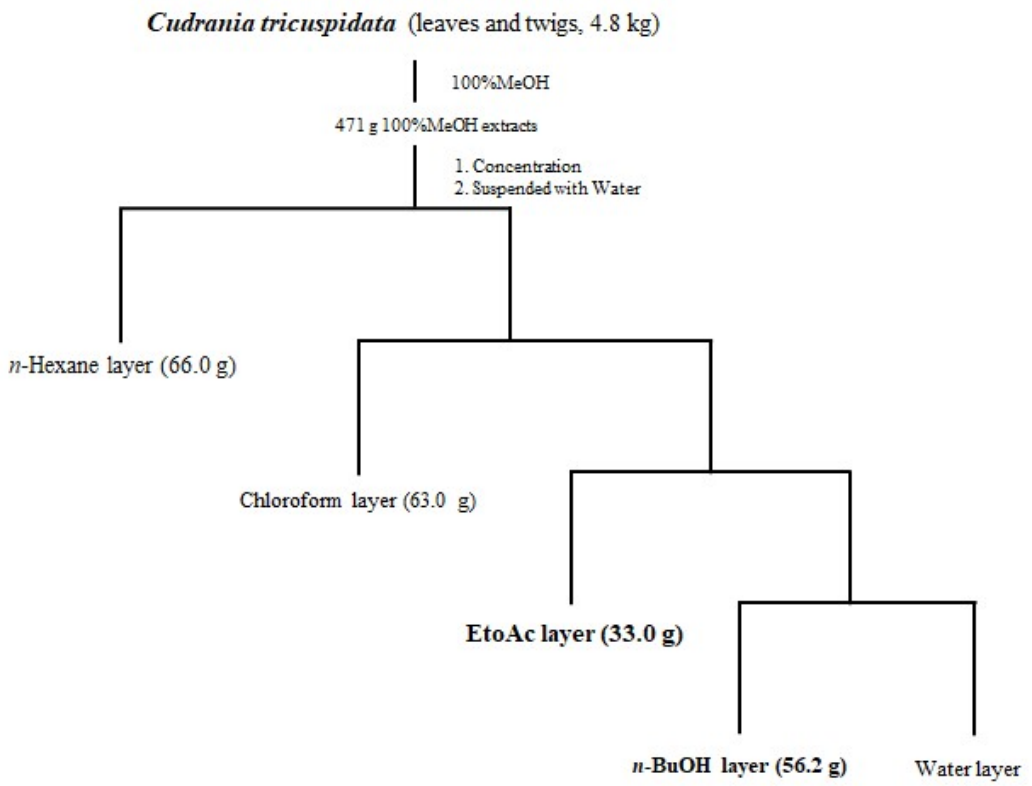
HPLC column : Hydrosphere C18 column (120 Å, i.d. 250 × 20 mm, 5 μm, YMC co., Ltd., Japan)

HypersilTM BDS C18 column (130 Å, i.d. 150 × 4.6 mm, 5 μm, Thermo ScientificTM, Germany)

Ultrasonicator : Branson 5510, UK

2.2. Method

The leaves and twigs of *C. tricuspidata* (4.8 kg) were extracted five times in 100%MeOH (total 80 L) with 90 minutes sonication each time, at room temperature. The methanolic crude extract (471 g) was concentrated at 40° C, in a rotary evaporator under reduced pressure. Then, it was suspended with H_2O, followed by partition with *n*-hexane, $CHCl_3$, EtOAc and *n*-BuOH successively.



Schematic Diagram 1. Extraction and fractionation of *C. tricupidata*

Part of the EtOAC fraction (33.0 g) was subjected to normal phase silica gel column chromatography (CC, 34 x 15.3 cm) with step gradient mixtures of Chloroform-MeOH(10:1 to 100%MeOH) to afford nine fractions (E.1-E.9).

Fraction E.2 (1.1 g) was subjected to MPLC (50%MeOH to 100%MeOH) to afford ten fractions (E2.1-E.2.10). Fraction E.2.2 (29.4 mg) was subjected to Sephadex LH-20 (100%MeOH) to afford five fractions (E.2.2.1-E.2.2.5). Fraction E.2.2.4 (12.5 mg) was purified with RP HPLC to give compound **10** (5.5 mg).

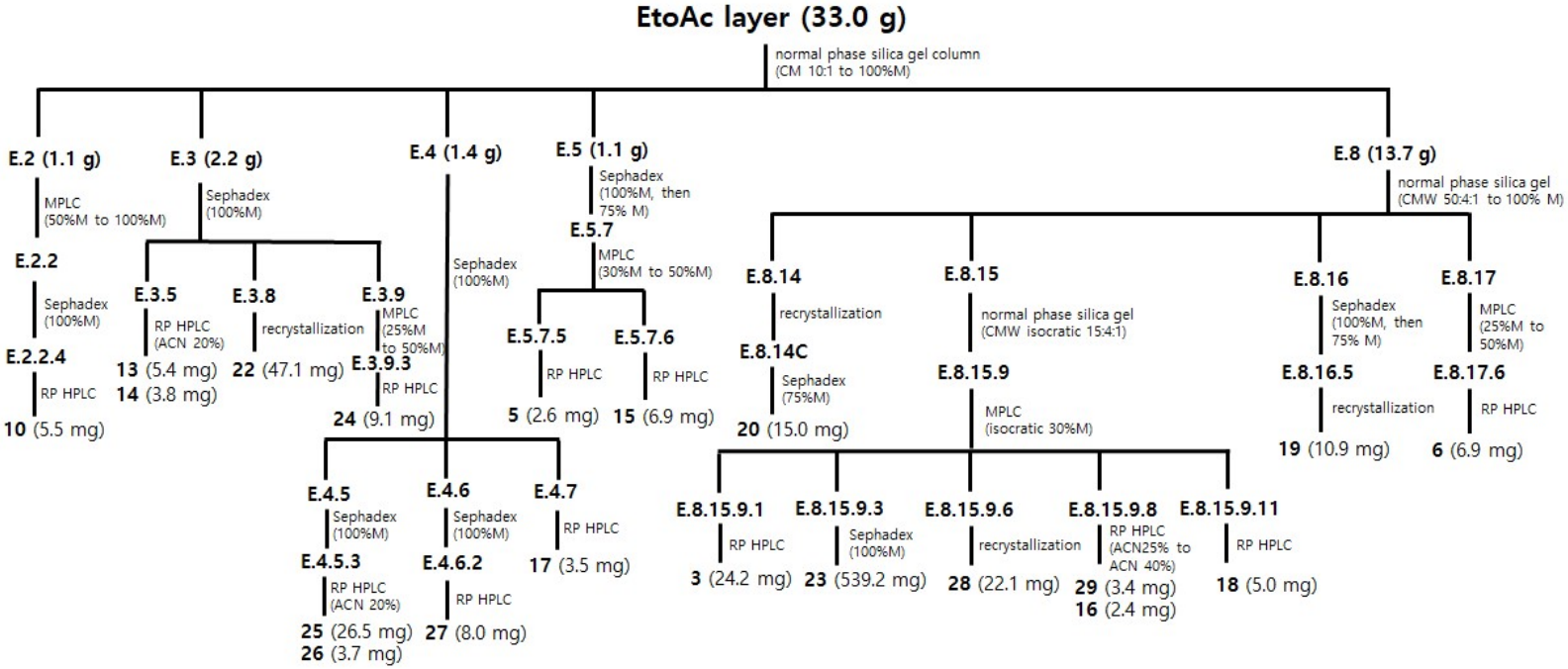
Fraction E.3 (2.2 g) was subjected to Sephadex LH-20 (100%MeOH) to afford nine fractions (E.3.1-E.3.9). Fraction E.3.5 (201.6 mg) was separated by RP HPLC (ACN15%) to give compound **13** (5.4 mg) and compound **14** (3.8 mg). Fraction E.3.8 (276.4 mg) was recrystallized in 100%MeOH to afford crystal, compound **22** (47.1 mg). Fraction E.3.9 (2.2 g) was subjected to Sephadex LH-20 (100%MeOH) to afford nine fractions (E.3.1-E.3.9). Fraction E.3.9 (576.0 mg) was subjected to MPLC (50%MeOH to 70%MeOH) to afford seven fractions (E.3.9.1-E.3.9.3). Fraction E.3.9.3 (21.9 mg) was purified with RP HPLC to give compound **24** (9.1 mg).

Fraction E.4 (1.4 g) was subjected to Sephadex LH-20 (100%MeOH) to afford eight fractions (E.4.1-E.4.8). Fraction E.4.5 (408.4 mg) was subjected to Sephadex LH-20 (100%MeOH) to afford eight fractions (E.4.5.1-E.4.5.8). Fraction E.4.5.3 (118.2 mg) was separated by RP HPLC (20% ACN) to give compound **25** (26.5 mg) and compound **26** (3.7 mg). Fraction E.4.6 (90.6 mg) was subjected to Sephadex LH-20 (100%MeOH) to afford five fractions (E.4.6.1-E.4.6.5). Fraction E.4.6.2 (43.5 mg) was purified with RP HPLC to give compound **27** (8.0 mg) E.4.7 (66.9 mg) was purified with RP HPLC to give compound **17** (3.5 mg).

Fraction E.5 (1.1 g) was subjected to Sephadex LH-20 (100%MeOH then, 75% MeOH) to afford nine fractions (E.5.1-E.5.9). Fraction E.5.7 (274.7 mg) was subjected to MPLC (30%MeOH to 50%MeOH) to afford eight fractions (E.5.7.1-E.5.7.8). Fraction E.5.7.5 (33.8 mg) was purified with RP HPLC to give compound **5** (2.6 mg). Fraction E.5.7.6 (34.6 mg) was purified with RP HPLC to give compound **15** (6.9 mg).

Fraction E.8 (13.7 g) was subjected to normal phase silica gel with step gradient mixtures of Chloroform-MeOH-H_2O (50:4:1 to 100%MeOH) to afford nineteen fractions (E.8.1-E.8.19). Fraciton E.8.14 (1.7 g) was recrystallized in 100%MeOH to afford E.8.14.C (39.2 mg). Fraciton E.8.14.C was subjected to Sephadex LH-20 (75%MeOH) to afford six fractions (E.8.14C.1-8.14C.6). Fraction E.8.14C.5 was compound **20** (15.0 mg). E.8.15 (5.3 g) was subjected to a normal silica column chromatography (Chloroform-MeOH-H_2O isocratic 15:4:1) to afford nine fractions (E.8.15.1-E.8.15.9). Fraction E.8.15.9 (2.8 g) was subjected to MPLC (isocratic MW 3:7) to afford twelve fractions (E.8.15.9.1-E.8.15.9.12). Fraction E.8.15.9.1 (58.6 mg) was purified with RP HPLC to give compound **3** (24.2mg). Fraction E.8.15.9.3 (762.7 mg) was subjected to Sephadex LH-20 (100%MeOH) to afford seven fractions (E.8.15.9.3.1-E.8.15.9.3.7). Fraction E.8.15.9.3.7 (539.2 mg) was recrystallized in 100%MeOH to afford crystal, compound **23** (32.4 mg). Fraction E.8.15.9.6 (63.5 mg) was recrystallized in 100%MeOH to afford crystal, compound **28** (22.1 mg). Fraction E.8.15.9.8 (33.4 mg) was separated by RP HPLC (25%ACN to 40%ACN) to afford compound **29** (3.4 mg) and compound **16** (2.4 mg). Fraction E.8.15.9.11 (95.7 mg) was purified with RP HPLC to give compound **18** (5.5 mg). Fraction E.8.16 (1.2 g) was subjected to Sephadex LH-20 (100%MeOH, then,

75%MeOH) to afford eight fractions (E.8.16.1-E.8.16.8). Fraction E.8.16.5 (36.6 mg) was recrystallized in 100%MeOH to afford crystal, compound **19** (10.9 mg). Fraction E.8.17 (719.1 mg) was subjected to MPLC (25%MeOH to 50%MeOH) to afford twelve fractions (E.8.17.1-E.8.17.12). Fraction E.8.17.6 (58.1 mg) was purified with RP HPLC to give compound **6** (6.9 mg).



Schematic Diagram 2. Isolation of compounds from EtOAC fraction of *C. tricupidata*

Part of BuOH fraction (56.2 g) was subjected to HP-20 (20%MeOH to 100%MeOH) to afford two fractions (BH.1- BH.2) and BH.2 was called BH.

Fraction BH (33.0 g) was subjected to normal phase silica gel column chromatography (CC, 34 x 15.3 cm) with step gradient mixtures of Chloroform-MeOH-Water (25:4:1 to 100%MeOH) to afford eleven fractions (BH.1-BH.11).

Fraction BH.2 (125.6 mg) was purified with RP HPLC to compound 8 (5.7 mg).

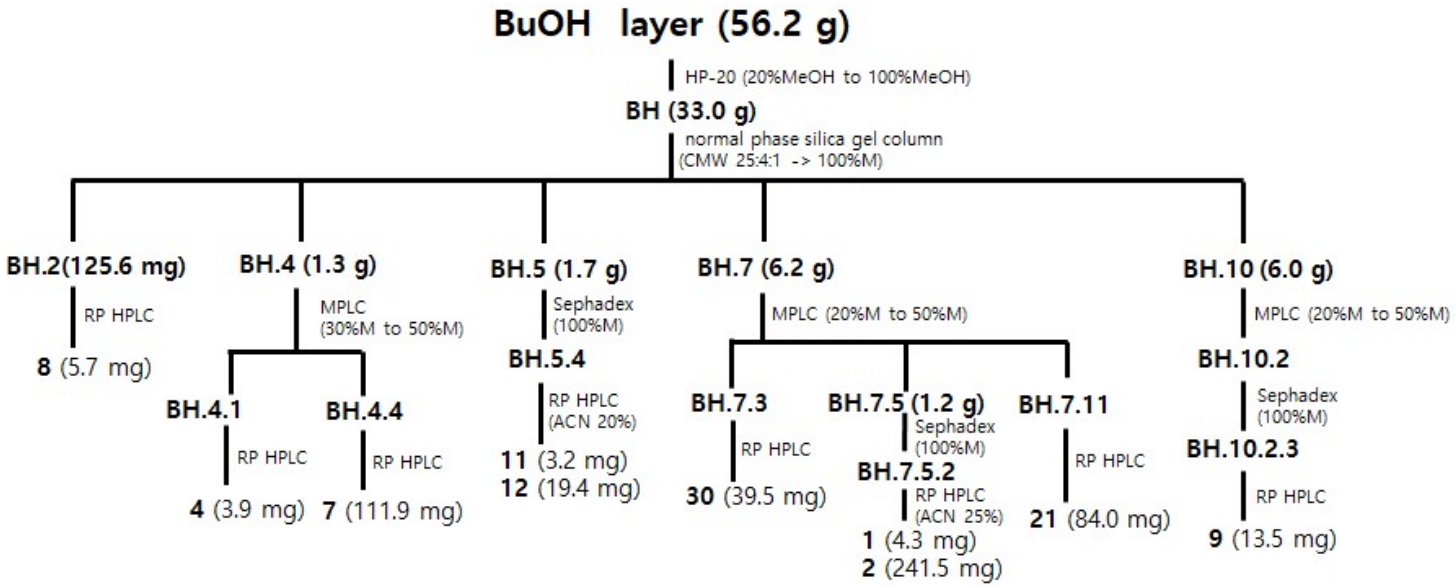
Fraction BH.4 (1.3 g) was subjected to MPLC (30%MeOH to 50%MeOH) to afford ten fractions (BH.4.1-BH.4.10). Fraction BH.4.1 (38.6 mg) was purified with RP HPLC to give compound **4** (3.9 mg). Fraction BH.4.4 (328.0 mg) was purified with RP HPLC to give compound **7**(111.9 mg).

Fraction BH.5 (1.7 g) was subjected to MPLC (20%MeOH to 50%MeOH) to afford seventeen fractions (BH.5.1-BH.5.17). Fraction BH5.4 (239.5 mg) was subjected to Sephadex LH-20 (100%MeOH) to afford seven fractions (BH.5.4.1-BH.5.4.7). Fraction BH.5.4.4 (82.8 mg) was separated by RP HPLC (20%MeOH) to afford compound **11** (3.2 mg) and compound **12** (19.4 mg).

Fraction BH.7 (6.2 g) was subjected to MPLC (20%MeOH to 50%MeOH) to afford twelve fractions (BH.7.1-BH.7.12). Fraction BH.7.3 (158.1 mg) was purified with RP HPLC to compound **30** (39.5 mg). Fraction BH.7.5 (1.2 g) was subjected to Sephadex LH-20 (100%MeOH) to afford eight fractions (BH.7.5.1-BH.7.5.8). Fraction BH.7.5.2 (606.7 mg) was separated by RP HPLC (25%ACN) to give compound **1** (4.3 mg) and compound **2** (241.5 mg). Fraction BH.7.11 (266.7 mg) was purified with RP HPLC to give compound **21** (84.0 mg).

Fraction BH 10 (6.0 g) was subjected to MPLC (20%MeOH to 50%MeOH) to afford ten fractions (BH10.1-BH.10.10). Fraction BH.10.2 (1.3 g) was subjected to

Sephadex LH-20 (100%MeOH) to afford five fractions (BH10.2.1-BH.10.2.5). Fraction BH10.2.3 (410.3 mg) was purified with RP HPLC to give compound **9** (13.5 mg).



Schematic Diagram 3. Isolation of compounds from *n*-butanol fraction of *C. tricupidata*

2.3. Spectroscopic and spectrometric data of isolated compounds

4'-glucopyranosyloxybenzyl-4-*O*-*β*-D-glucopyranosyloxy-3,5-dimethoxybenzoate (**1**)

Pale yellow amorphous powder

$C_{28}H_{36}O_{16}$

$[\alpha]_D^{20}$ -12.4 (*c* 0.10, MeOH)

IR ν_{max} : 3365, 2922, 1717, 1593, 1509, 1460, 1416, 1377, 1333, 1325, 1235, 1072 cm^{-1}

HRMS (ESI-QTOF): *m/z* 627.1942 $[M-H]^-$ (calcd. for $C_{28}H_{35}O_{16}$, 627.1925)

^1H NMR (DMSO-d_6, 500 MHz) : See Table 1

^{13}C NMR (DMSO-d_6, 125 MHz) : See Table 1

Bis [4-*O*-*β*-D-glucopyranosyloxy)benzyl] 3-hydroxy-3-methylglutarate (**2**)

Colorless amorphous powder

$C_{32}H_{42}O_{17}$

$[\alpha]_D^{20}$ -15.8 (*c* 0.10, MeOH)

IR ν_{max} : 3390, 2927, 1726, 1613, 1509, 1382, 1346, 1235, 1077 cm^{-1}

HRMS (ESI-QTOF): *m/z* 697.2343 $[M-H]^-$ (calcd. for $C_{32}H_{41}O_{17}$, 697.2344)

^1H NMR (CD_3OD, 300 MHz) : See Table 2

^{13}C NMR (CD_3OD, 75 MHz) : See Table 2

Table 1. ^{1}H NMR and ^{13}C NMR data of compound **1** (***δ*** in ppm)

position	δ_C	δ_H (***J*** **in Hz)**
1	124.4	
2	107.2	7.24 s
3	152.4	
4	138.6	
5	152.4	
6	107.2	7.24 s
7	165.2	
1'	129.4	
2'	129.7	7.39 d (8.6)
3'	116.2	7.04 d (8.6)
4'	157.3	
5'	116.2	7.04 d (8.6)
6'	129.7	7.39 d (8.6)
7'	65.9	5.28 s
1"	101.8	5.13 d (7.1)
2"	74.1	3.0-3.7
3"	76.6	3.0-3.7
4"	69.8	3.0-3.7
5"	77.2	3.0-3.7
6"	60.7	3.0-3.7
1"'	100.3	4.86 d (7.4)
2"'	73.2	3.0-3.7
3"'	76.6	3.0-3.7
4"'	69.7	3.0-3.7
5"'	77.0	3.0-3.7
6"'	60.7	3.0-3.7
3, 5 -OCH_3	56.4	3.80 s

Table 2. ^{1}H NMR and ^{13}C NMR data of compound **2** (***δ*** in ppm)

position	δ_C	δ_H (***J*** **in Hz)**
1	172.3	
2	46.2	2.64 m
3	70.9	
4	46.2	2.64 m
5	172.3	
6	27.9	1.28 s
1'	131.3	
2'	130.9	7.25 d (8.7)
3'	117.7	7.04 d (8.7)
4'	159.0	
5'	117.7	7.04 d (8.7)
6'	130.9	7.25 d (8.7)
7'	66.9	5.0 s
1"	131.3	
2"	130.9	7.25 d (8.7)
3"	117.7	7.04 d (8.7)
4"	159.0	
5"	117.7	7.04 d (8.7)
6"	130.9	7.25 d (8.7)
7"	66.9	5.0 s
1"'	102.1	4.87 d (7.6)
2"'	74.8	3.3-3.5
3"'	77.9	3.3-3.5
4"'	71.3	3.3-3.5
5"'	78.1	3.3-3.5
6"'	62.5	3.68 dd (12.1, 5.0), 3.86 dd (12.1, 1.9)
1""	102.1	4.87 d (7.6)
2""	74.8	3.3-3.5

3""	77.9	3.3-3.5
4""	71.3	3.3-3.5
5""	78.1	3.3-3.5
6""	62.5	3.68 dd (12.1, 5.0), 3.86 dd (12.1, 1.9)

Gastrodin (**3**)

Colorless needles

$C_{13}H_{18}O_7$

$[\alpha]_D^{20}$ -19.4 (*c* 0.10, MeOH)

IR ν_{max} : 3500-3200, 1615, 1590, 1575 cm^{-1}

ESIMS: *m/z* 309.1$[M+Na]^+$

^1H NMR (CD_3OD, 400 MHz) : See Table 3

^{13}C NMR (CD_3OD, 100 MHz) : See Table 3

p-hydroxybenzaldehyde 4-*O*-*β*-D-glucopyranoside (**4**)

White amorphous powder

$C_{13}H_{16}O_7$

$[\alpha]_D^{20}$ -14.8 (*c* 0.10, MeOH)

ESIMS: *m/z* 307.1 $[M+Na]^+$

^1H NMR (CD_3OD, 400 MHz) : See Table 4

^{13}C NMR (CD_3OD, 75 MHz) : See Table 4

Table 3. ^{1}H NMR and ^{13}C NMR data of compound **3** (***δ*** in ppm)

position	δ_C	δ_H (***J*** **in Hz)**
1	136.6	
2	129.4	7.27 d (8.5)
3	117.6	7.07 d (8.5)
4	158.5	
5	117.6	7.07 d (8.5)
6	129.4	7.27 d (8.5)
7	64.8	4.53 s
1'	102.4	4.88 d (7.5)
2'	74.9	3.3-3.5
3'	78.0	3.3-3.5
4'	71.4	3.3-3.5
5'	78.1	3.3-3.5
6'	62.5	3.69 dd (12.1, 5.1), 3.88 dd (12.1, 1.7)

Table 4. ^{1}H NMR and ^{13}C NMR data of compound **4** (***δ*** in ppm)

position	δ_C	δ_H (***J*** **in Hz)**
1	132.5	
2	132.8	7.87 d (8.7)
3	117.8	7.24 d (8.7)
4	164.0	
5	117.8	7.24 d (8.7)
6	132.8	7.87 d (8.7)
1'	101.5	5.05 d (7.6)
2'	74.6	3.3-3.9
3'	77.9	3.3-3.9
4'	71.2	3.3-3.9
5'	78.3	3.3-3.9
6'	62.4	3.3-3.9
-CHO	192.8	9.86

3,4,5-trimethoxyphenyl-1-*O*-*β*-D-glucopyranoside (**5**)

White amorphous powder.

$C_{15}H_{22}O_9$

$[\alpha]_D^{20}$ -15.9 (*c* 0.10, MeOH)

ESIMS: *m/z* 369.2 $[M+Na]^+$

^1H NMR (CD_3OD, 300 MHz) : See Table 5

^{13}C NMR (CD_3OD, 75 MHz) : See Table 5

Cudrabibenzyl A (**6**)

White amorphous powder.

$C_{21}H_{24}O_{10}$

$[\alpha]_D^{20}$ -36.8 (*c* 0.20, MeOH)

IR ν_{max}: 3307, 1662, 1610, 1514, 1258, 1074 cm^{-1}

HRMS (ESI-QTOF): *m/z* 435.1292 $[M-H]^-$

^1H NMR (CD_3OD, 300 MHz) : See Table 6

^{13}C NMR (CD_3OD, 75 MHz) : See Table 6

Table 5. ^{1}H NMR and ^{13}C NMR data of compound **5** (***δ*** in ppm)

position	δ_C	δ_H (***J*** **in Hz)**
1	154.8	
2	96.1	6.49 s
3	156.0	
4	134.4	
5	156.0	
6	96.1	6.49 s
1'	103.2	4.81 d (7.6)
2'	75.0	3.3-3.5
3'	78.1	3.3-3.5
4'	71.7	3.3-3.5
5'	78.4	3.3-3.5
6'	62.7	3.66 dd (12.0, 6.0), 3.92 dd (12.0, 2.2)
3,5-OCH_3	56.5	3.83 s
4-OCH_3	61.2	3.71 s

Table 6. ^{1}H NMR and ^{13}C NMR data of compound **6** (***δ*** in ppm)

position	δ_C	δ_H (***J*** **in Hz)**
1	134.3	
2	130.4	7.00 d (8.5)
3	116.0	6.68 d (8.5)
4	156.4	
5	116.0	6.68 d (8.5)
6	130.4	7.00 d (8.5)
7	38.5	2.76 m
8	40.3	3.16 m
1'	148.7	
2'	108.1	6.41 d (2.1)
3'	166.0	
4'	103.1	6.47 d (2.1)
5'	162.8	
6'	112.4	
1"	101.4	4.86 d (7.4)
2"	74.7	3.3-3.9
3"	77.9	3.3-3.9
4"	71.3	3.3-3.9
5"	78.2	3.3-3.9
6"	62.4	3.3-3.9
-COOH	174.5	

(6*S*, 9*R*) – Roseoside (**7**)

Colorless amorphous powder

$C_{19}H_{30}O_8$

$[\alpha]_D^{20}$ +34.6 (*c* 0.10, MeOH)

IR ν_{max} : 3404, 2971, 2932, 1652, 1598, 1441, 1372, 1278, 1160, 1057, 1032 cm^{-1}

HRMS (ESI-QTOF): *m/z* 385.1855 $[M-H]^-$

^1H NMR (CD_3OD, 300 MHz) : See Table 7

^{13}C NMR (CD_3OD, 75 MHz) : See Table 7

Table 7. ^{1}H NMR and ^{13}C NMR data of compound **7** (***δ*** in ppm)

position	δ_C	δ_H (***J*** **in Hz)**
1	42.4	
2	50.6	
3	201.1	
4	127.1	5.82 s
5	167.1	
6	79.9	
7	131.4	5.84 m
8	135.2	5.82 m
9	77.2	4.38 m
10	21.2	1.29 d (6.2)
11	23.4	1.00 s
12	24.7	0.99 s
13	19.6	1.88 d (1.3)
1'	102.6	4.31 d (7.8)
2'	75.0	3.1-3.4
3'	77.9	3.1-3.4
4'	71.5	3.1-3.4
5'	78.0	3.1-3.4
6'	62.7	3.59 dd (11.7, 5.4) 3.81 dd (11.7, 1.8)

3-*O*-caffeoyl-2-*C*-methyl-D-erythrono-1,4-lactone (**8**)

Dark yellow amorphous powder

$C_{14}H_{14}O_7$

$[\alpha]_D^{20}$ -8.5 (*c* 0.10, MeOH)

IR ν_{max} : 3409, 2976, 1780, 1706, 1631, 1604, 1519, 1451, 1363, 1273, 1163, 1118, 1033.66 cm^{-1}

ESIMS: *m/z* 293.1 $[M-H]^-$

^1H NMR (CD_3OD, 300 MHz) : See Table 8

^{13}C NMR (CD_3OD, 75 MHz) : See Table 8

Chlorogenic acid (**9**)

Colorless amorphous powder

$[\alpha]_D^{20}$ -34.0 (*c* 0.10, MeOH)

$C_{16}H_{18}O_9$

IR ν_{max} : 3389, 2956, 2928, 2857, 2626, 1685, 1638, 1614, 1528, 1517, 1442, 1384, 1289, 1252, 1190, 1158, 1133, 1114, 1086, 1038 cm^{-1}

ESIMS: *m/z* 353.1 $[M-H]^-$

^1H NMR (CD_3OD, 300 MHz) : See Table 8

^{13}C NMR (CD_3OD, 75 MHz) : See Table 8

Table 8. ^{1}H NMR and ^{13}C NMR data of compound **8-9 (*δ* in ppm)**

	8		**9**	
position	δ_C	δ_H (***J* in Hz**)	δ_C	δ_H (***J* in Hz**)
1	180.0		73.5	
2	74.4		38.2	2.18 m
3	76.9	5.29 m	72.0	5.33 m
4	71.9	4a=4.61 dd (11.2, 4.2)	72.0	3.72 m
		4b=4.32 dd (11.2, 0.7)		
5	23.2	1.5 s	71.3	4.17 m
6			38.7	2.25 m ,
				2.05 m
1'	128.5		127.7	
2'	116.0	7.05 d (1.8)	115.2	6.26 d (15.9)
3'	147.6		147.0	7.56 d (15.9),
4'	150.6		149.5	
5'	117.3	6.77 d (8.2)	116.4	7.05 d (2.0)
6'	124.0	6.96 dd (8.2, 1.8)	122.9	
7'	148.8	7.62 d (15.9)	147.0	
8'	115.1	6.32 d (15.9)	115.1	6.78 d (8.2)
9'	168.8		168.6	6.95 dd (8.2, 2.0)
-COOH			177.0	

Umbelliferone (**10**)

White amorphous powder

$C_9H_6O_3$

$[\alpha]_D^{20}$ +54.7 (*c* 0.10, MeOH)

ESIMS: *m/z* 161.1 $[M-H]^-$

^1H NMR (CD_3OD, 300 MHz) : See Table 9

^{13}C NMR (CD_3OD, 75 MHz) : See Table 9

Skimmin (**11**)

White amorphous powder

$C_{15}H_{16}O_8$

$[\alpha]_D^{20}$ -20.5 (*c* 0.10, MeOH)

ESIMS: *m/z* 347.2 $[M+Na]^+$

^1H NMR (CD_3OD, 300 MHz) : See Table 9

^{13}C NMR (CD_3OD, 75 MHz) : See Table 9

Esculin (**12**)

White amorphous powder

$C_{15}H_{16}O_9$

$[\alpha]_D^{20}$ -27.5 (*c* 0.10, MeOH)

ESIMS: *m/z* 339.1 $[M-H]^-$

^1H NMR (CD_3OD, 300 MHz) : See Table 9

^{13}C NMR (CD_3OD, 75 MHz) : See Table 9

Table 9. ^{1}H NMR and ^{13}C NMR data of compound **10-12** (***δ*** in ppm)

	10		**11**		**12**	
position	δ_C	δ_H (***J*** **in Hz**)	δ_C	δ_H (***J*** **in Hz**)	δ_C	δ_H (***J*** **in Hz**)
1						
2	163.6		163.1		163.6	
3	112.3	6.18 d (9.5)	114.3	6.18 d (9.5)	113.0	6.21 d (9.4)
4	146.0	7.85 d (9.5)	145.5	7.89 d (9.5)	146.0	7.84 d (9.4)
5	130.6	7.45 d (8.5)	130.4	7.56 d (9.3)	116.5	7.42 s
6	114.4	6.79 dd (8.5, 2.3)	115.2	7.09, m	153.2	
7	163.1		162.1		144.4	
8	103.3	6.71 d (2.3)	105.0	7.07, m	104.5	6.79 s
9	157.2		156.7		152.5	
10	113.1		115.2		112.8	
1'			102.9	5.03 d (7.6)	104.2	4.85 d (7.4)
2'			74.8	3.3-3.5	74.8	3.3-3.6
3'			77.9	3.3-3.5	77.4	3.3-3.6
4'			71.2	3.3-3.5	71.3	3.3-3.6
5'			78.3	3.3-3.5	78.5	3.3-3.6
6'			62.5	3.70 dd (12.1, 5.7), 3.91 dd (12.1, 2.1)	62.5	3.72 dd (12.1, 5.6), 3.94 dd (12.1, 2.0)

C-veratroylglycol (**13**)

Pale yellow amorphous powder

$C_{10}H_{12}O_5$

$[\alpha]_D^{20}$ -8.4 (*c* 0.10, MeOH)

HRMS (ESI-QTOF): m/z 211.0598 $[M-H]^-$

^1H NMR (CD_3OD, 300 MHz) : See Table 10

^{13}C NMR (CD_3OD, 75 MHz) : See Table 10

2,3-dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-1-propanone (**14**)

Pale yellow amorphous powder

$C_{11}H_{14}O_6$

$[\alpha]_D^{20}$ +4.5 (*c* 0.20, MeOH)

ESIMS: m/z 241.1 [M-H]-

^1H NMR (CD3OD, 300 MHz) : See Table 10

^{13}C NMR (CD3OD, 75 MHz) : See Table 10

4-hydroxy benzoic acid (**15**)

White amorphous powder

$[\alpha]_D^{20}$ +49.1 (*c* 0.10, MeOH)

$C_7H_6O_3$

ESIMS: *m/z* 137.1 $[M-H]^-$

^1H NMR (CD_3OD, 300 MHz) : See Table 11

^{13}C NMR (CD_3OD, 75 MHz) : See Table 11

Methyl-4-hydroxy benzoate (**16**)

White amorphous powder

$C_8H_8O_3$

$[\alpha]_D^{20}$ +82.9 (*c* 0.10, MeOH)

ESIMS: *m/z* 151.1 $[M-H]^-$

^1H NMR ($CDCl_3$, 300 MHz) : See Table 11

^{13}C NMR ($CDCl_3$, 75 MHz) : See Table 11

Table 10. ^{1}H NMR and ^{13}C NMR data of compound **13-14 (*δ* in ppm)**

	13		**14**	
position	***δ*** $_{C}$	***δ*** $_{H}$ **(*J* in Hz)**	***δ*** $_{C}$	***δ*** $_{H}$ **(*J* in Hz)**
1	199.5		199.6	
2	75.5	5.11 dd (5.1,3.8)	75.6	5.12 dd (5.1, 3.9)
3	66.3	3a=3.73 dd (11.7, 5.1) 3b=3.89 dd (11.7, 3.8)	66.3	3a=3.74 (11.6, 5.2), 3b=3.86 m
1'	128.0		126.7	
2'	112.4	7.57 brs	107.7	7.34 s
3'	149.2		149.1	
4'	153.8		143.0	
5'	115.9	6.88 d 8.5	149.1	
6'	125.0	7.6 m	107.7	7.34 s
3-OCH_3	56.4	3.91 s	56.9	3.9 s
5-OCH_3			56.9	3.9 s

Table 11. ^{1}H NMR and ^{13}C NMR data of compound **15-16 (*δ* in ppm)**

	15		**16**	
position	***δ*** $_{C}$	***δ*** $_{H}$ **(*J* in Hz)**	***δ*** $_{C}$	***δ*** $_{H}$ **(*J* in Hz)**
1	122.9		122.9	
2	133.0	7.86 d (8.8)	131.9	7.94 d (8.8)
3	116.0	6.80 d (8.8)	115.1	6.84 d (8.8)
4	163.3		159.6	
5	116.0	6.80 d (8.8)	115.1	6.84 d (8.8)
6	133.0	7.86 d (8.8)	131.9	7.94 d (8.8)
7	170.2		166.8	
1'			51.9	3.86 s

Quercetin (**17**)

Dark yellow amorphous powder

$C_{15}H_{10}O_7$

$[\alpha]_D^{20}$ -65.6 (*c* 0.10, MeOH)

ESIMS: *m/z* 301.1 $[M-H]^-$

^1H NMR (DMSO-d_6, 300 MHz) : See Table 12

^{13}C NMR (DMSO-d_6, 75 MHz) : See Table 13

Quercetin-3-*O*-*β*-D-glucopyranoside (**18**)

Yellow amorphous powder

$C_{21}H_{20}O_{12}$

$[\alpha]_D^{20}$ -8.3 (*c* 0.10, MeOH)

ESIMS: *m/z* 463.1 $[M-H]^-$

^1H NMR (DMSO-d_6, 300 MHz) : See Table 12

^{13}C NMR (DMSO-d_6, 75 MHz) : See Table 13

Quercetin-7-*O*-*β*-D-glucopyranoside (**19**)

Yellow amorphous powder

$C_{21}H_{20}O_{12}$

$[\alpha]_D^{20}$ -89.0 (*c* 0.10, MeOH)

ESIMS: *m/z* 463.1 $[M-H]^-$

^1H NMR (DMSO-d_6, 300 MHz) : See Table 12

^{13}C NMR (DMSO-d_6, 75 MHz) : See Table 13

Kaempferol-7-*O*-*β*-D-glucopyranoside (**20**)

Yellow amorphous powder

$C_{21}H_{20}O_{11}$

$[\alpha]_D^{20}$ -15.2 (*c* 0.10, MeOH)

ESIMS: *m/z* 447.1 $[M-H]^-$

^1H NMR (DMSO-d_6, 300 MHz) : See Table 12

^{13}C NMR (DMSO-d_6, 75 MHz) : See Table 13

Nicotiflorin (**21**)

Yellow amorphous powder

$C_{27}H_{30}O_{15}$

$[\alpha]_D^{20}$ -4.6 (*c* 0.20, MeOH)

ESIMS: *m/z* 617.2 $[M+Na]^+$

^1H NMR (DMSO-d_6, 300 MHz) : See Table 12

^{13}C NMR (DMSO-d_6, 75 MHz) : See Table 13

Table 12. ^{1}H NMR data of compound **17-21 (*δ* in ppm)**

	17	**18**	**19**	**20**	**21**
position	**δ_H (*J* in Hz)**	**δ_H (*J* in Hz)**	**δ_H (*J* in Hz)**	**δ_H (*J* in Hz)**	**δ_H (*J* in Hz)**
1					
2					
3					
4					
5					
6	6.18 brs	6.06 brs	6.42 d (2.1)	6.42 d (2.1)	6.41 d (2.0)
7					
8	6.40 brs	6.26 brs	6.76 d (2.1)	6.80 d (2.1)	6.20 d (2.0)
9					
10					
1'					
2'	7.67 brs	7.57 m	7.72 d (2.2)	8.07 d (8.9)	7.98 d (8.9)
3'				6.94 d (8.9)	6.89 d (8.9)
4'					
5'	6.87 d (8.4)	6.90 d (9.0)	6.90 d (8.5)	6.94 d (8.9)	6.89 d (8.9)
6'	7.54 m	7.55 m	7.55 dd (8.5, 2.2)	8.07 d (8.9)	7.98 d (8.9)
1"		5.42 d (7.3)	5.08 d (7.4)	5.06 d (7.2)	5.31 d (7.4)
2"		3.0-3.7	3.0-3.7	3.0-3.7	3.0-3.7
3"		3.0-3.7	3.0-3.7	3.0-3.7	3.0-3.7
4"		3.0-3.7	3.0-3.7	3.0-3.7	3.0-3.7
5"		3.0-3.7	3.0-3.7	3.0-3.7	3.0-3.7
6"		3.0-3.7	3.0-3.7	3.0-3.7	3.0-3.7
1"'					4.38 d (1.2)
2"'					3.0-3.9
3"'					3.0-3.9
4"'					3.0-3.9
5"'					3.0-3.9
6"'					0.98 d (6.2)

Table 13. ^{13}C NMR data of compound **17-21 (*δ* in ppm)**

	17	**18**	**19**	**20**	**21**
position	δ_C	δ_C	δ_C	δ_C	δ_C
1					
2	146.8	156.3	147.8	147.5	156.5
3	135.8	133.3	136.1	136.1	133.2
4	175.8	177.4	176.0	176.0	177.3
5	160.7	161.2	160.3	160.3	161.2
6	98.1	98.1	98.7	99.8	99.1
7	163.9	164.1	162.6	162.6	164.2
8	93.3	93.3	94.2	94.4	94.1
9	156.1	156.1	155.5	155.7	156.8
10	103.0	104.0	104.6	104.7	104.3
1'	121.9	121.6	121.8	121.5	120.9
2'	115.0	115.2	115.3	129.6	130.9
3'	145.1	144.8	145.0	115.4	115.1
4'	147.7	148.4	147.5	159.3	160.2
5'	115.6	116.2	115.1	115.4	115.1
6'	119.9	121.1	120.0	129.6	131.2
1"		100.8	99.8	99.8	101.3
2"		74.1	73.1	73.1	74.2
3"		76.5	76.4	76.4	76.4
4"		69.9	69.5	69.6	70.3
5"		77.6	77.1	77.1	76.1
6"		61.0	60.6	60.6	66.9
1"'					100.8
2"'					70.3
3"'					70.7
4"'					72.1
5"'					68.3
6"'					17.8

Aromadendrin (**22)**

Yellow amorphous powder

$C_{15}H_{12}O_6$

$[\alpha]_D^{20}$ +4.5 (*c* 0.20, MeOH)

ESIMS: *m/z* 287.1 $[M-H]^-$

^1H NMR (DMSO-d_6, 300 MHz) : See Table 14

^{13}C NMR (DMSO-d_6, 75 MHz) : See Table 14

Aromadendrin-7-*O*-*β*-D-glucopyranoside (**23**)

Yellow amorphous powder

$[\alpha]_D^{20}$ -18.7 (*c* 0.20, MeOH)

ESIMS: *m/z* 449.1 $[M-H]^-$

$C_{21}H_{22}O_{11}$

^1H NMR (DMSO-d_6, 300 MHz) : See Table 14

^{13}C NMR (DMSO-d_6, 75 MHz) : See Table 14

Gericudranin E (**24)**

Yellow amorphous powder

$[\alpha]_D^{20}$ +14.0 (*c* 0.20, MeOH)

ESIMS: *m/z* 393.1 $[M-H]^-$

$C_{22}H_{18}O_7$

^1H NMR (CD_3OD, 300 MHz) : See Table 15

^{13}C NMR (CD_3OD, 75 MHz) : See Table 15

Taxifolin (**25)**

Dark yellow amorphous powder

$[\alpha]_D^{20}$ +11.9 (*c* 0.10, MeOH)

ESIMS: *m/z* 303.1 $[M-H]^-$

$C_{15}H_{12}O_7$

^1H NMR (CD_3OD, 300 MHz) : See Table 16

^{13}C NMR (CD_3OD, 75 MHz) : See Table 16

Dihydromorin (**26)**

Dark yellow amorphous powder

$[\alpha]_D^{20}$ +18.0 (*c* 0.20, MeOH)

ESIMS: *m/z* 303.1 $[M-H]^-$

$C_{15}H_{12}O_7$

^1H NMR (CD_3OD, 300 MHz) : See Table 16

^{13}C NMR (CD_3OD, 75 MHz) : See Table 16

Table 14. ^{1}H NMR and ^{13}C NMR data of compound **22-23 (*δ* in ppm)**

	22		**23**	
position	δ_C	δ_H (***J* in Hz**)	δ_C	δ_H (***J* in Hz**)
1				
2	82.9	5.05 d (11.4)	83.1	5.13 d (11.4)
3	71.5	4.58 d (11.4)	73.0	4.67, m
4	197.9		198.7	
5	163.3		162.7	
6	96.1	5.87 d (2.2)	96.8	6.14 d (2.2)
7	166.8		165.4	
8	95.1	5.92 d (2.2)	95.4	6.17 d (2.2)
9	162.6		162.4	
10	100.5		102.1	
1'	127.6		127.4	
2'	129.5	7.32 d (8.5)	129.5	7.33 d (8.6)
3'	115.0	6.79 d (8.5)	115.0	6.80 d (8.6)
4'	157.8		157.8	
5'	115.0,	6.79 d (8.5)	115.0	6.80 d (8.6)
6'	129.5	7.32 d (8.5)	129.5	7.33 d (8.6)
1"			99.6	4.97 d (7.3)
2"			73.0	3.0-3.6
3"			76.4	3.0-3.6
4"			69.5	3.0-3.6
5"			77.1	3.0-3.6
6"			60.6	3.0-3.6

Table 15. ^{1}H NMR and ^{13}C NMR data of compound **24** (***δ*** in ppm)

	24	
position	δ_C	δ_H (***J*** **in Hz**)
1		
2	85.7	4.95 d (11.6)
3	74.5	4.53 d (11.6)
4	199.4	
5	163.1	
6	111.3	
7	167.1	
8	96.3	5.94 s
9	163.2	
10	102.4	
1'	130.1	
2'	131.1	7.34 d (8.6)
3'	116.8	6.82 d (8.6)
4'	159.9	
5'	116.8	6.82 d (8.6)
6'	131.1	7.34 d (8.6)
1"	28.3	3.76 s
2"	134.4	
3"	131.3	7.09 d (8.6)
4"	116.3	6.61 d (8.6)
5"	156.8	
6"	116.3	6.61 d (8.6)
7"	131.3	7.09 d (8.6)

Table 16. ^{1}H NMR and ^{13}C NMR data of compound **25-26 (*δ* in ppm)**

	25		**26**	
position	δ_C	δ_H (***J* in Hz**)	δ_C	δ_H (***J* in Hz**)
1				
2	85.1	4.91 d (11.5)	80.0	5.39 d (11.4)
3	73.7	4.50 d (11.5)	72.5	4.79 d (11.4)
4	198.4		198.9	
5	164.5		168.5	
6	96.3	5.88 d (1.9)	96.1	5.87 d (2.1)
7	168.7		164.9	
8	97.3	5.92 d (1.9)	97.1	5.91 d (2.1)
9	165.3		165.3	
10	101.8		101.9	
1'	129.8		115.4	
2'	115.9	6.96 d (1.5)	158.6	
3'	146.3		103.6	6.34 m
4'	147.1		160.1	
5'	116.1	6.80 d (8.1)	107.8	6.34 m
6'	120.9	6.85 dd (8.1, 1.5)	130.8	7.22 d (9.0)

Orobol (**27**)

Dark yellow amorphous powder

$C_{15}H_{10}O_6$

$[\alpha]_D^{20}$ +15.5 (*c* 0.20, MeOH)

ESIMS m/z 285.0 $[M-H]^-$

^1H NMR (CD_3OD, 300 MHz) : See Table 17

^{13}C NMR (CD_3OD, 75 MHz) : See Table 18

Orobol-7-*O*-*β*-D-glucopyranoside (**28**)

Dark yellow amorphous powder

$C_{21}H_{20}O_{11}$

$[\alpha]_D^{20}$ -7.7 (*c* 0.10, MeOH)

ESIMS: *m/z* 447.1 $[M-H]^-$

^1H NMR (DMSO-d_6, 300 MHz) : See Table 17

^{13}C NMR (DMSO-d_6, 75 MHz) : See Table 18

Ambocin (**29**)

Colorless amorphous powder

$C_{26}H_{28}O_{14}$

$[\alpha]_D^{20}$ -28.5 (*c* 0.10, MeOH)

ESIMS: *m/z* 563.1 $[M-H]^-$

^1H NMR (CD_3OD, 300 MHz) : See Table 17

^{13}C NMR (CD_3OD, 75 MHz) : See Table 18

5-methoxy-8-glucopyranosyl-genistein (**30**)

Yellow amorphous powder

$C_{22}H_{28}O_{10}$

$[\alpha]_D^{20}$ -19.3 (*c* 0.10, MeOH)

ESIMS: *m/z* 445.1 $[M-H]^-$

^1H NMR (CD_3OD, 300 MHz) : See Table 17

^{13}C NMR (CD_3OD, 75 MHz) : See Table 18

Table 17. ^{1}H NMR data of compound **27-30 (*δ* in ppm)**

	27	**28**	**29**	**30**
position	**δ_H (*J* in Hz)**	**δ_H (*J* in Hz)**	**δ_H (*J* in Hz)**	**δ_H (*J* in Hz)**
1				
2	8.03 s	8.4 s	8.13 s	7.97s
3				
4				
5				
6	6.21 d (1.9)	6.47 d (1.9)	6.46 (2.0)	6.44, s
7				
8	6.33 d (1.9)	6.71 d (1.9)	6.73 (2.0)	
9				
10				
1'				
2'	7.02 brs	7.02 d (1.9)	7.4 (8.5)	7.31 (8.6)
3'			6.83 (8.5)	6.80 (8.6)
4'				
5'	6.83 m	6.78 d (8.2)	6.83 (8.5)	6.80 (8.6)
6'	6.83 m	6.83 dd (8.2, 1.9)	7.4 (8.5)	7.31 (8.6)
1"		5.07 d (7.2)	5.04 (7.2)	4.99 d (9.9)
2"		3.1-3.9	3.1-4.0	3.3-4.2
3"		3.1-3.9	3.1-4.0	3.3-4.2
4"		3.1-3.9	3.1-4.0	3.3-4.2
5"		3.1-3.9	3.1-4.0	3.3-4.2
6"		3.1-3.9	3.1-4.0	3.3-4.2
1"'			4.81 d (3.1)	
2"'			3.4-4.0	
3"'			3.4-4.0	
4"'			3.4-4.0	
5"'			3.4-4.0	
-OCH_3				3.84 s

Table 18. ^{13}C NMR data of compound **27-30 (*δ* in ppm)**

	27	**28**	**29**	**30**
position	δ_C	δ_C	δ_C	δ_C
1				
2	154.8	154.5	154.6	153.0
3	123.8	121.4	122.5	127.3
4	182.2	180.5	180.5	178.7
5	163.8	161.6	161.5	163.1
6	100.1	99.5	99.8	98.3
7	165.9	162.9	162.8	164.0
8	94.7	94.5	94.5	106.4
9	159.6	157.1	157.2	159.2
10	106.3	106.1	106.1	110.3
1'	124.8	122.7	121.0	125.1
2'	117.4	116.5	130.1	132.2
3'	146.2	144.9	115.1	116.8
4'	146.8	145.6	157.5	159.2
5'	116.3	115.4	115.1	116.8
6'	121.6	120.0	130.1	132.2
1"		100.8	99.6	73.9
2"		73.1	73.3	76.5
3"		76.4	76.4	80.8
4"		69.6	69.9	72.5
5"		77.2	75.6	83.4
6"		60.6	67.7	63.5
1"'			109.4	
2"'			75.9	
3"'			78.7	
4"'			73.0	
5"'			63.2	
5-OCH3				57.2

Chapter3. Results and Discussion

3.1. Compound 1

Compound **1** was obtained as pale yellow amorphous powder with molecular formula $C_{28}H_{36}O_{16,}$ based on the *m/z* 627.1942 $[M-H]^-$ in HRMS (ESI-QTOF). The ^1H NMR spectrum exhibited one 1,3,4,5-tetrasubstituted benzene ring [δ_H 7.24 (2H, s, H-2 and H-6)] and another 1,4-disubstituted benzene ring [δ_H 7.39 (2H, d , J = 8.6Hz, H-2' and H-6'), δ_H 7.04 (2H, d , J = 8.6Hz, H-3' and H-5')] with one oxygenated methylene at 5.28 (2H, s, H-7). It also exhibited the signals of two methoxy groups at δ_H 3.77 (3H, s, 3-OCH_3 and 3H, s, 5-OCH_3) and two anomeric protons at δ 5.10 (1H, d, J = 7.1Hz, H-1''), δ_H 4.86 (1H, d, J = 7.4Hz, H-1'''). The ^{13}C NMR spectrum exhibited ester group at δ_C 165.2ppm (C-7), along with strong IR absorption peak at 1717 cm^{-1}. It also showed two glucosyl moieties [δ_C 101.8 (C-1''), δ_C 74.1 (C-2''), δ_C 76.6 (C-3''), δ_C 69.8 (C-4''), δ_C 77.2 (C-5''), δ_C 60.7 (C-6''), δ_C 100.3 (C-1'''), δ_C 73.2 (C-2'''), δ_C 76.6 (C-3'''), δ_C 69.7 (C-4'''), δ_C 77.0 (C-5'''), δ_C 60.7 (C-6''')]. HMBC correlation from H-2', H-6' to C-7' and from H-7' to C-7 and from H-2, H-6 to C-7 indicated benzyl benzoate moiety. The methoxy groups were assigned by HMBC correlation from 3-OCH_3 to C-3, from 5-OCH_3 to C-5. Two glucosyl units were located at C-4 by the HMBC correlation from H-1'' to C-7'' and at C-4' by the HMBC correlation from H-1''' to C-7'''. Two glucosyl moieties were identified as D-glucose by HPLC analysis of acid hydrolysate of **1**. (Tanaka et al.2007) Thus, the structure of Compound **1** was determined as 4'-glucopyranosyloxybenzyl-4-*O*-*β*-D-glucopyranosyloxy-3,5-dimethoxybenzoate. It

was isolated for the first time from nature

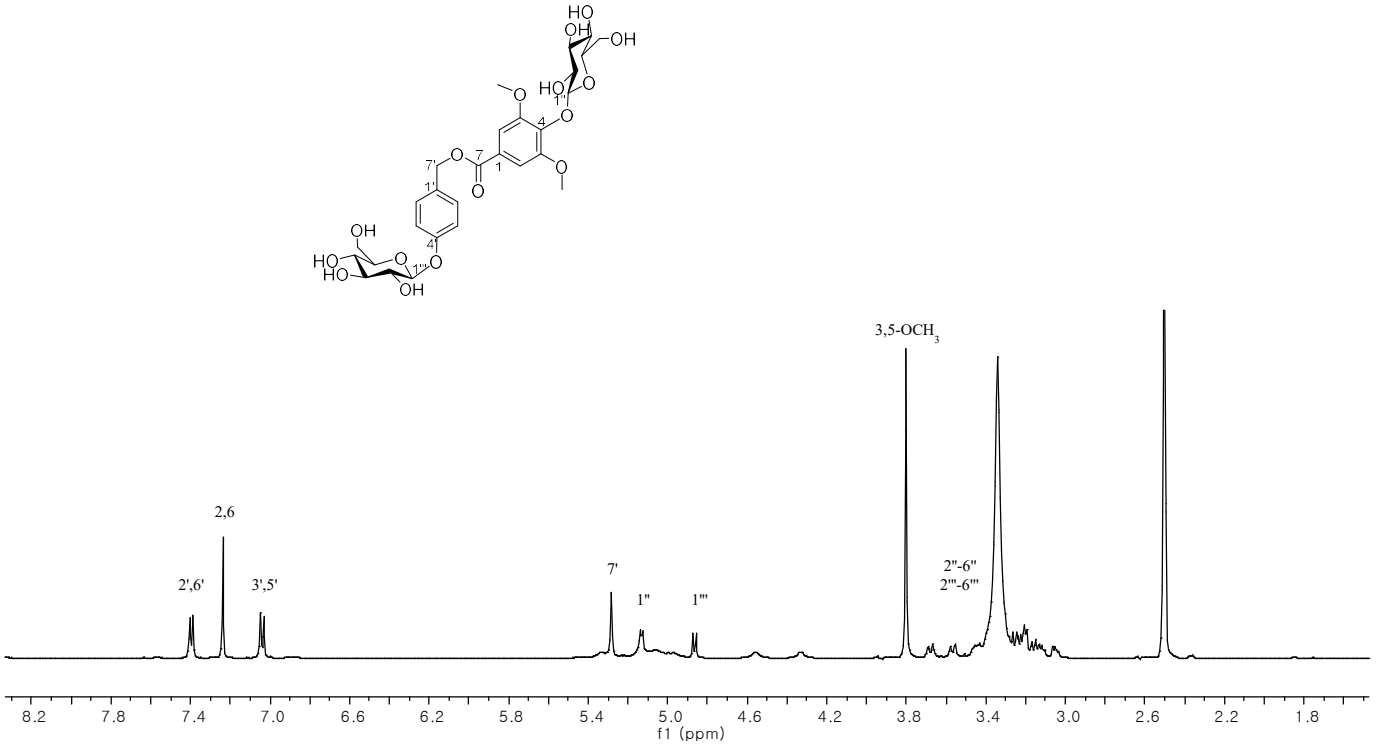


Figure 1. ^{1}H NMR spectrum of compound **1** (500 MHz, DMSO-d_6)

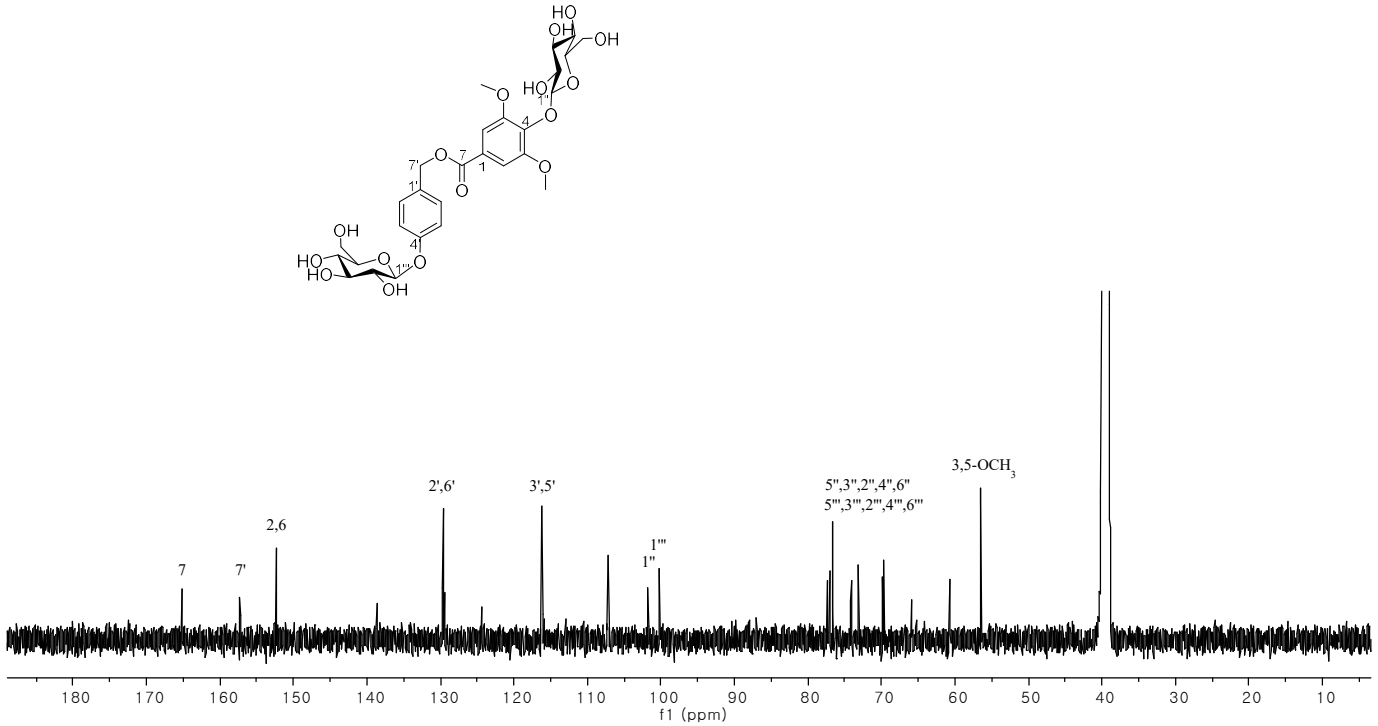


Figure 2. ^{13}C NMR spectrum of compound **1** (125 MHz, DMSO-d_6)

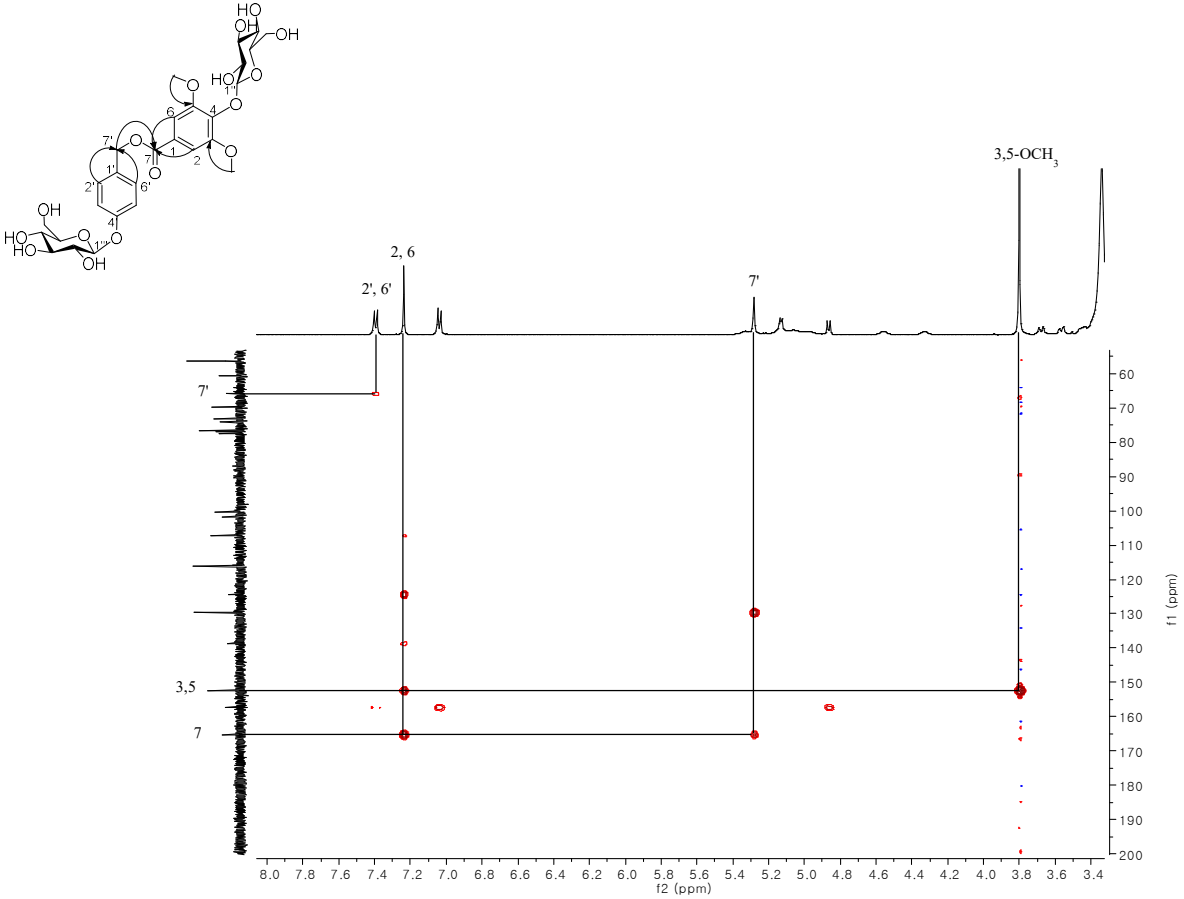


Figure 3. HMBC spectrum of compound **1** (400 MHz, DMSO-d_6)

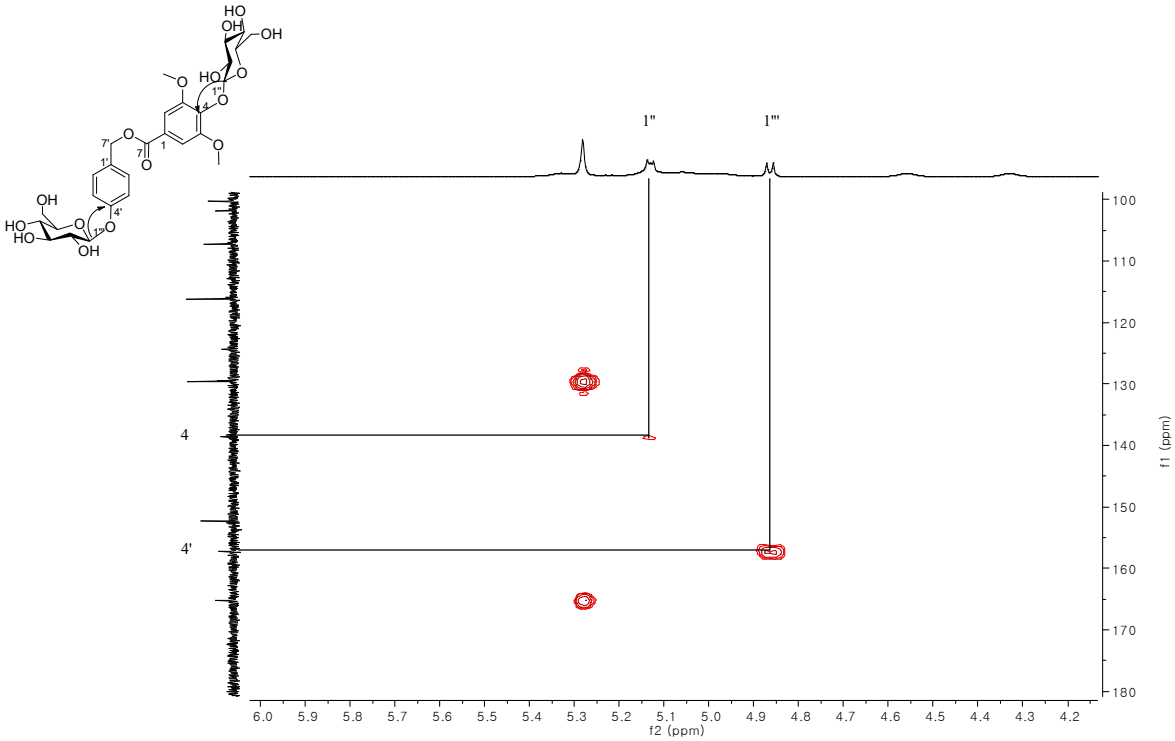


Figure 4. HMBC spectrum of compound **1** (400 MHz, DMSO-d_6)

3.2 Compound 2

Compound **2** was obtained as colorless amorphous powder. Molecular formula of compound 2 was $C_{32}H_{42}O_{17}$, based on HRMS (ESI-QTOF) at m/z 697.2343 $[M-H]^-$. However, ^{13}C NMR spectrum indicated that compound 2 must be a symmetric dimer, as ^{13}C NMR carbon resonances were observed for only 15 carbon atoms. The ^{1}H NMR spectrum exhibited two 1,4-disubstituted benzene rings [δ_H 7.25 (4H, d , J = 8.7Hz, H-2', H-2" H-6' and H-6"), δ_H 7.04 (4H, d , J = 8.7Hz, H-3', H-3" H-5' and H-5")] with two oxygenated methylene at δ_H 5.00 (2H, s, H-7). It also exhibited the signals two anomeric protons at δ_H 4.86 (1H, d, J = 7.4Hz, H-1'" and H-1""). In ^{13}C NMR spectrum, the signal at δ_C 172.3ppm, along with strong IR absorption peak at 1726cm^{-1} indicated ester groups at C-1, C-5. The ^{13}C NMR spectrum also showed two glucosyl moieties [δ_C 102.1 (C-1'" and C-1""), δ_C 74.8 (C-2'" and C-2""), δ_C 77.9 (C-3'" and C-3""), δ_C 71.3 (C-4'" and C-4""), δ_C 78.1 (C-5'" and C-5""), δ_C 62.5 (C-6'" and C-6"")]. HMBC correlations from H-6 to C-2, C-3 and C-4, from H-2 to C-1 and from H-4 to C-5 indicated HMG moiety. The HMG group was located between two benzyl groups by the HMBC correlation from H-2' and H-6' to C-1, from H-2" and H-6" to C-5. Two glucosyl units were located at C-4' by the HMBC correlation from H-1'" to C-4" by the HMBC correlation from H-1"" to C-4"". Two glucosyl moieties were identified as D-glucose by HPLC analysis of acid hydrolysate of **2**. (Tanaka et al.2007) Thus, the structure of Compound **2** was determined as Bis [4-*O*-(*β*-D-glucopyranosyloxy)benzyl] 3-hydroxy-3-methylglutarate. It was isolated for the first time from nature.

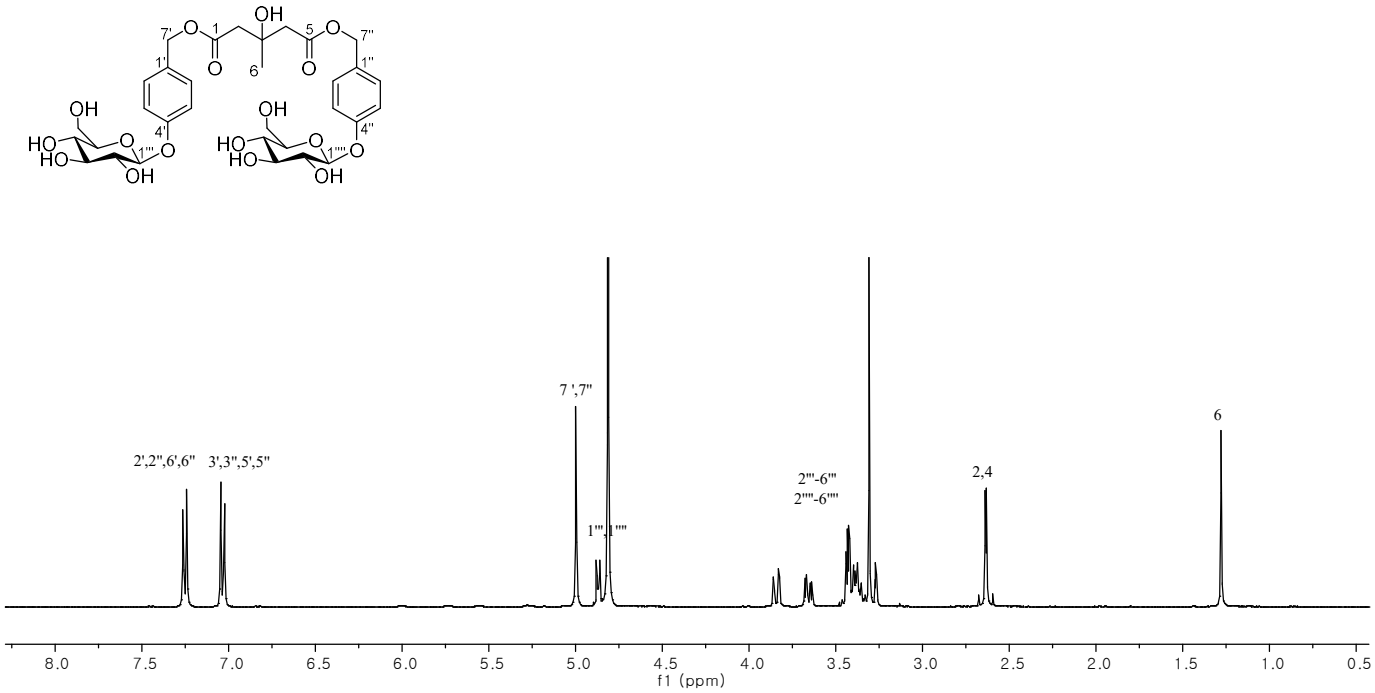


Figure 5. ^{1}H NMR spectrum of compound **2** (300MHz, CD_3OD)

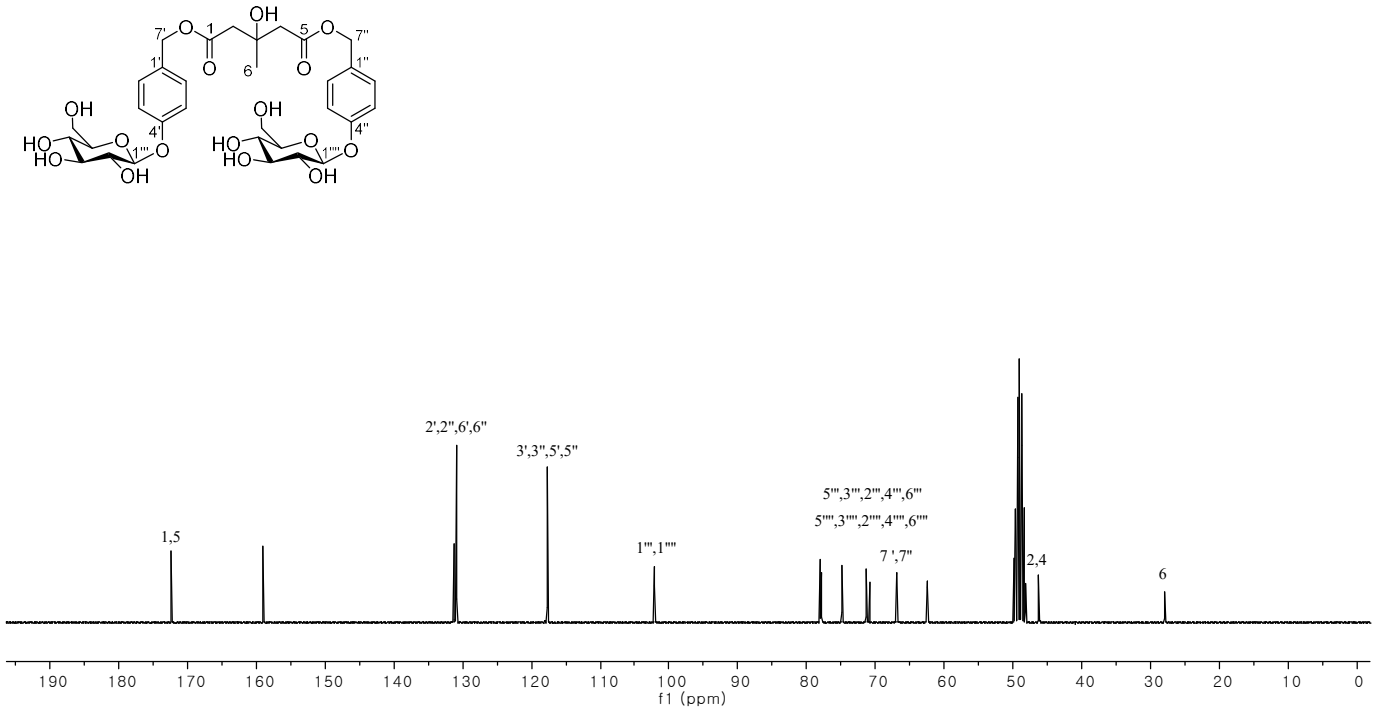


Figure 6. ^{13}C NMR spectrum of compound **2** (75MHz, CD_3OD)

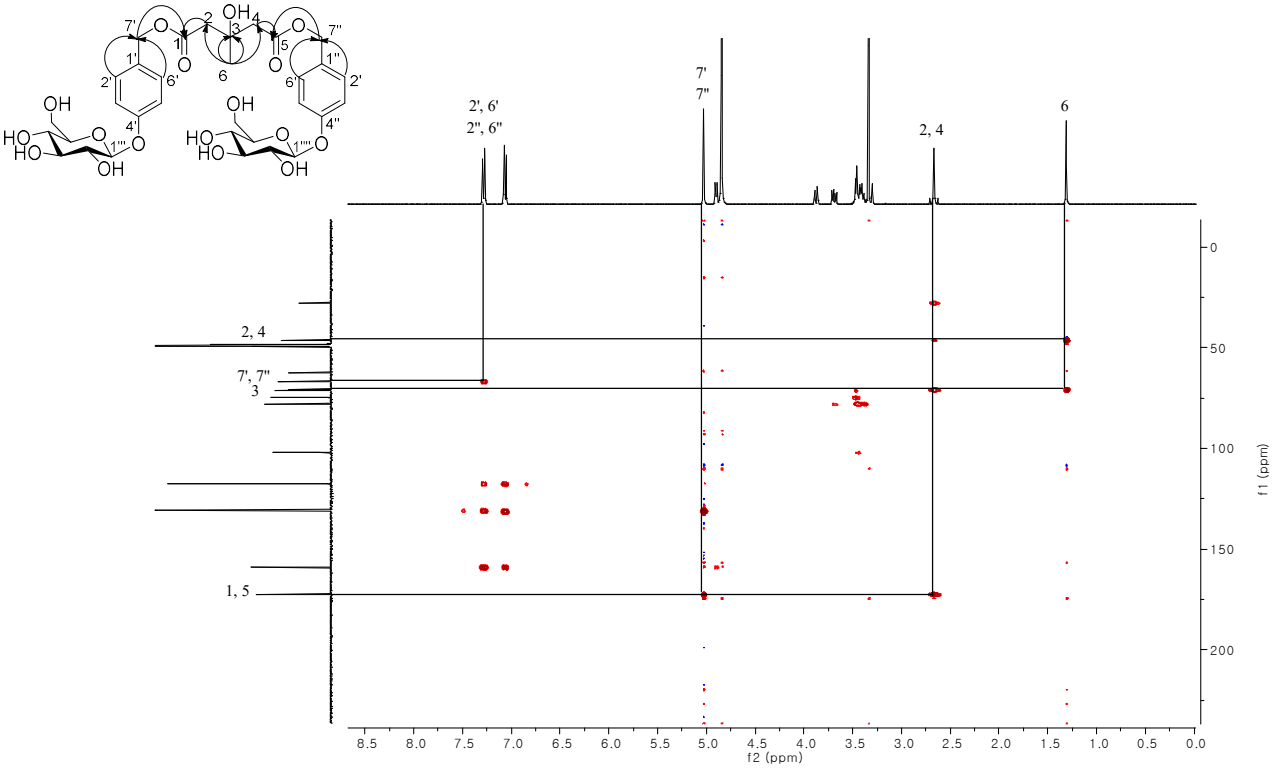


Figure 7. HMBC spectrum of compound **2** (400 MHz, CD_3OD)

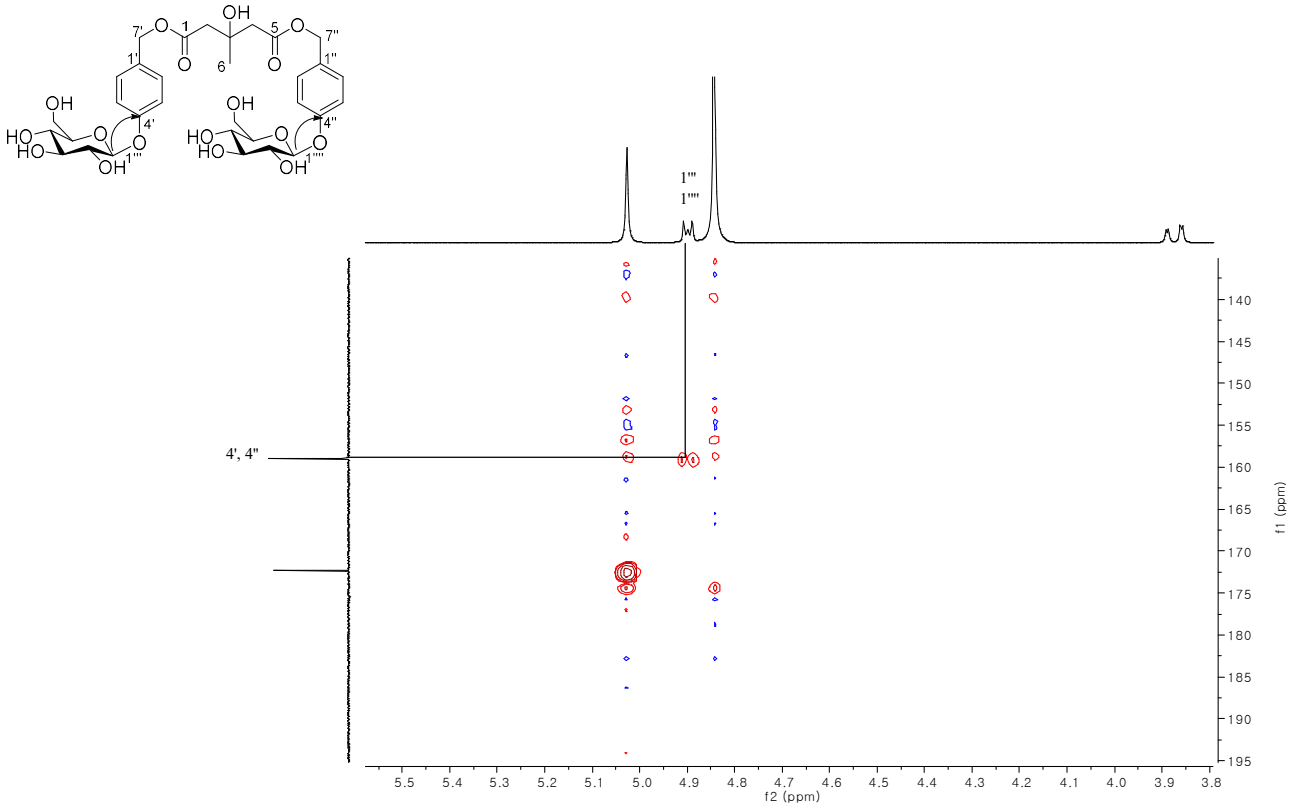


Figure 8. HMBC spectrum of compound **2** (400 MHz, CD_3OD)

3.3 Compound 3

Compound **3** was obtained as white needles with molecular formula $C_{13}H_{18}O_7$, based on the *m/z* 309.1$[M+Na]^+$ in ESIMS. The ^1H NMR spectrum of **3** revealed the presence of partial structure, whose signals were observed as 1,4-disubstituted benzene ring [δ_H 7.27 (2H, d, J = 8.5Hz, H-2 and H-6) and δ_H 7.07 (2H, d, J = 8.5Hz, H-3 and H-5)] with one oxygenated methylene [4.53 (2H, s, H-7)]. It also exhibited the signal of an anomeric protons at δ_H 4.88 (1H, d, J = 7.5Hz, H-1'). The ^{13}C NMR spectrum showed glucosyl moiety [δ_C 102.4 (C-1'), δ_C 74.9 (C-2'), δ_C 78.0 (C-3'), δ_C 71.4 (C-4'), δ_C 78.1 (C-5'), δ_C 62.5 (C-6')]. With ^1H and ^{13}C NMR spectra, the structure of compound **3** was assigned as gastrodin. (Chen et al. 2016)

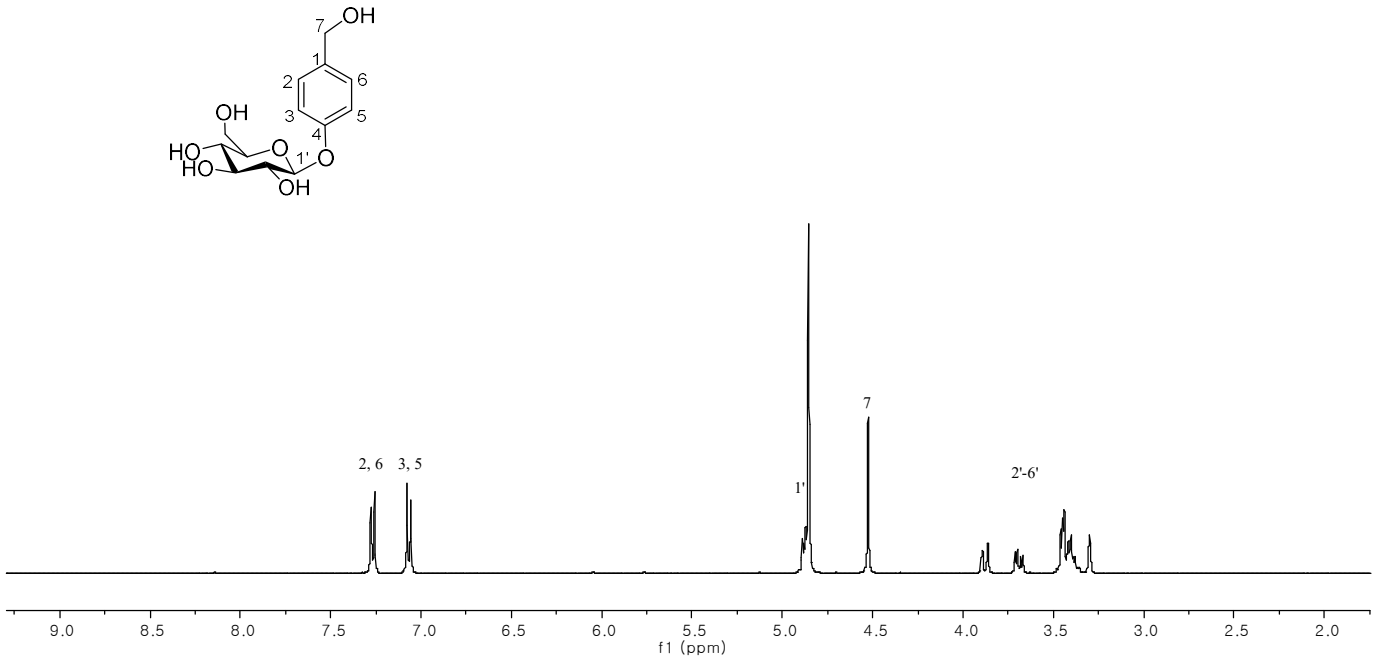


Figure 9. ^{1}H NMR spectrum of compound **3** (400 MHz, CD_3OD)

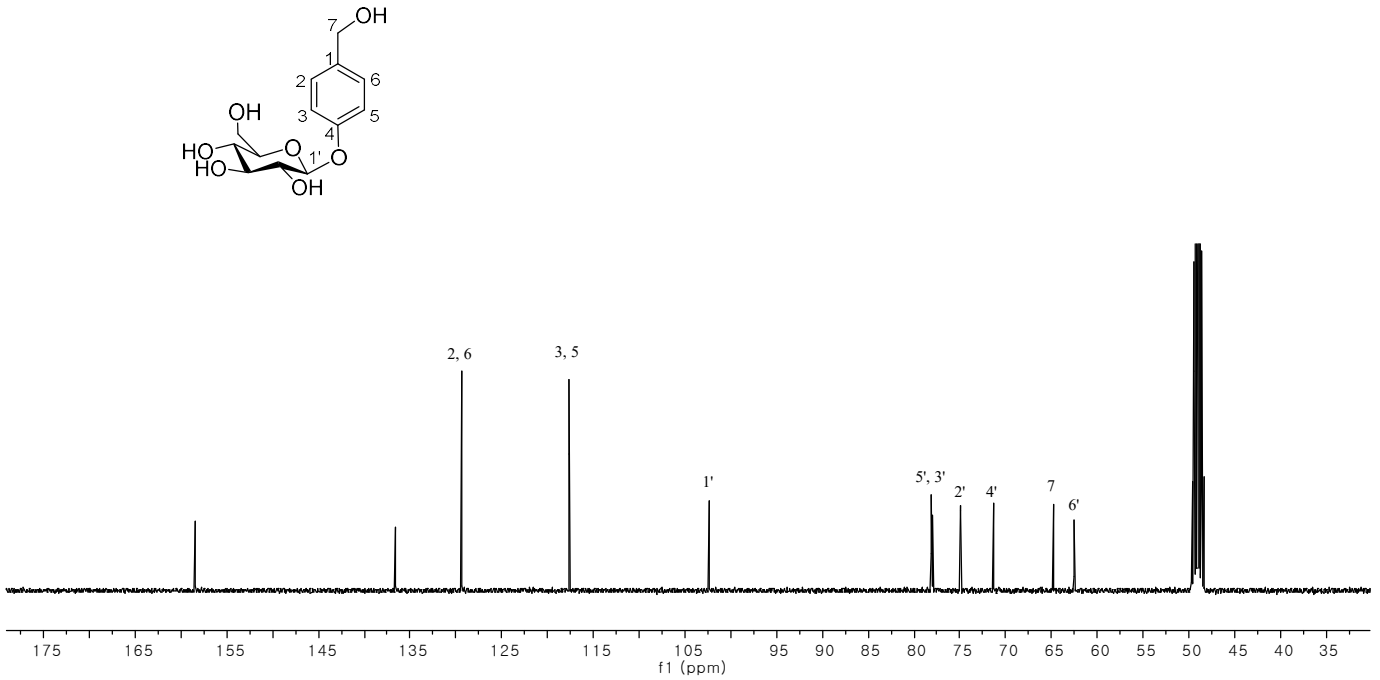


Figure 10. ^{13}C NMR spectrum of compound **3** (100 MHz, CD_3OD)

3.4. Compound 4

Compound **4** was obtained as white amorphous powder with molecular formula $C_{13}H_{16}O_7$, based on the *m/z* 307.1 $[M+Na]^+$ in ESIMS. The ^1H NMR spectrum of **4** exhibited 1,4-disubstituted benzene ring, whose signals were observed at δ_H 7.87 (2H, d, J = 8.7Hz, H-2 and H-6) and δ_H 7.24 (2H, d, J = 8.7Hz, H-3 and H-5). It also exhibited the signal of aldehyde proton at δ_H 9.86 (1H, s, -CHO) and the signal of an anomeric proton at δ_H 5.05 (1H, d, J = 7.6Hz, H-1'). The ^{13}C NMR spectrum showed glucosyl moiety [δ_C 101.5 (C-1'), δ_C 74.6 (C-2'), δ_C 77.9 (C-3'), δ_C 71.2 (C-4'), δ_C 78.3 (C-5'), δ_C 62.4 (C-6')]. With ^1H and ^{13}C NMR spectra, the structure of compound **4** was assigned as *p*-hydroxybenzaldehyde-4-*O*-*β*-D-glucopyranoside. (Morikawa et al. 2006)

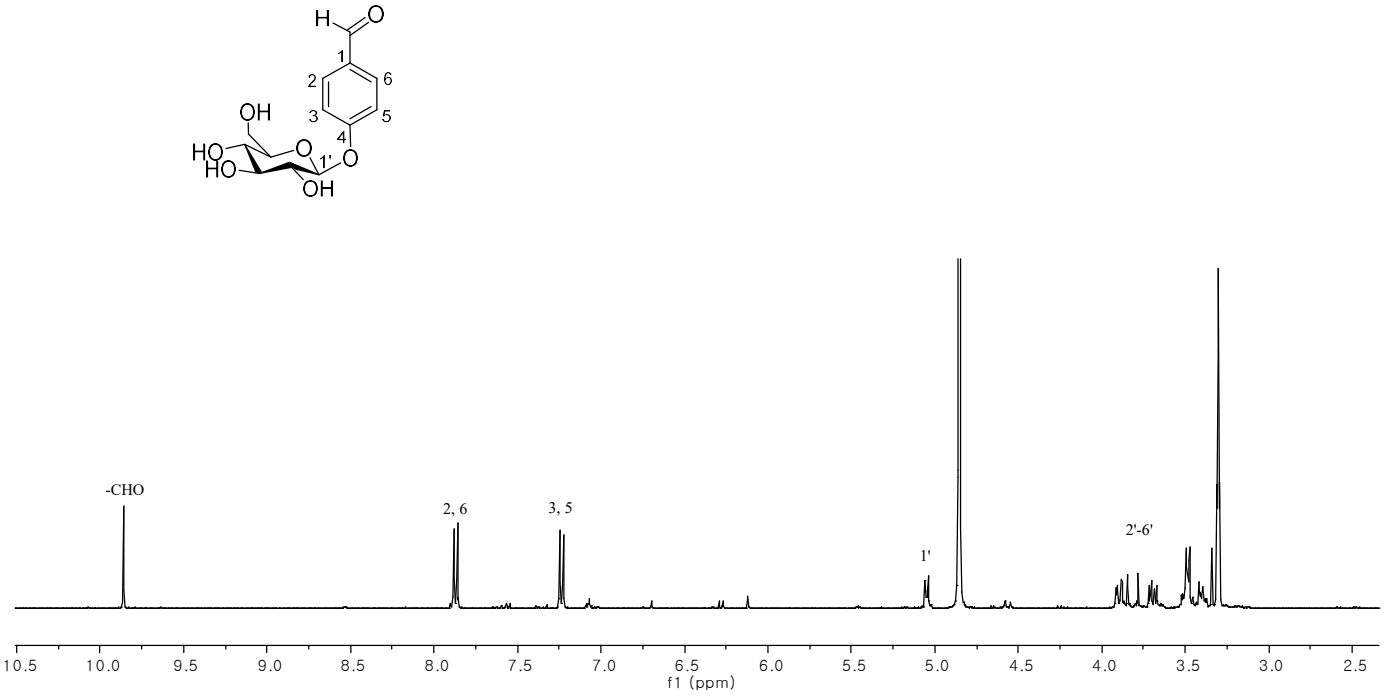


Figure 11. ^{1}H NMR spectrum of compound **4** (300MHz, CD_3OD)

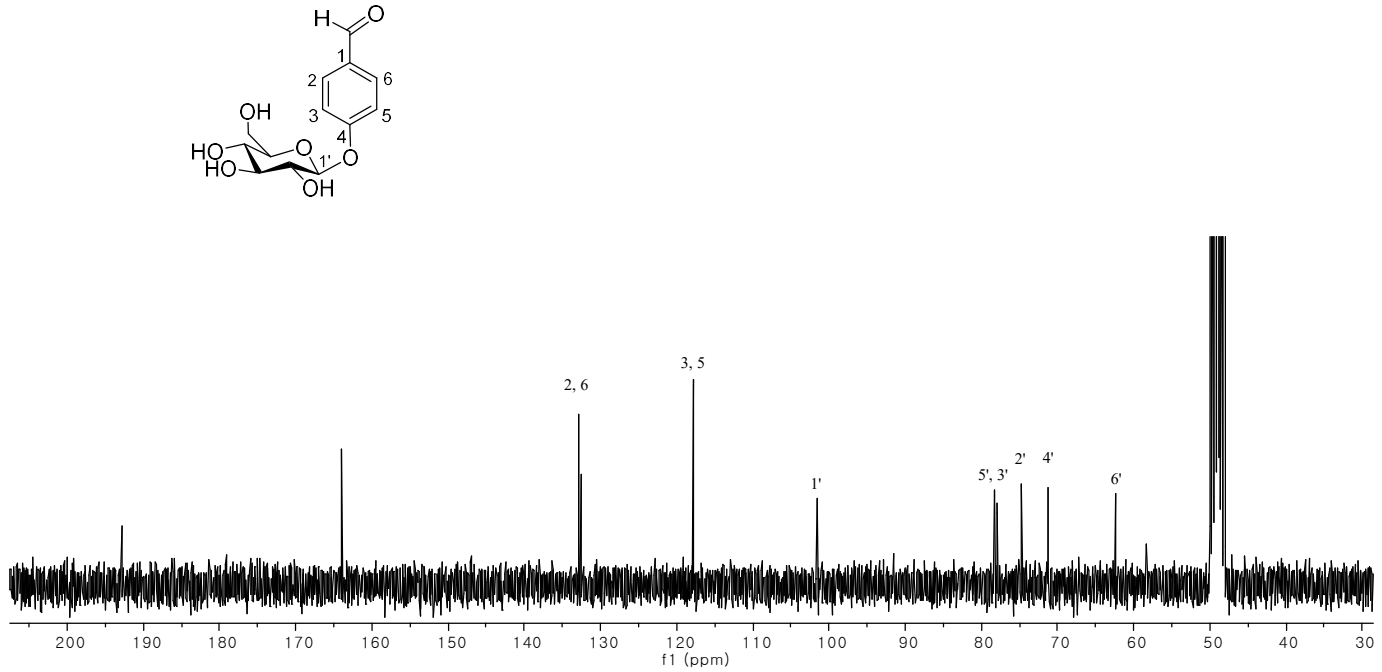


Figure 12. ^{13}C NMR spectrum of compound **4** (75 MHz, CD_3OD)

3.5. Compound 5

Compound **5** was obtained as white amorphous powder with molecular formula $C_{15}H_{22}O_9$, based on the *m/z* 369.2 $[M+Na]^+$ in ESIMS. The ^1H NMR spectrum of **5** exhibited 1,3,4,5-tetrasubstituted benzene ring, whose signals were observed at δ_H 6.49 (2H, s, H-2 and H-6). It also exhibited the presence of three methoxy groups [δ_H 3.83 (6H, s, 3, 5-OCH_3) and δ_H 3.71 (3H, s, 4-OCH_3)] and the signal of an anomeric proton at δ_H 4.81 (1H, d, J = 7.6Hz, H-1'). The ^{13}C NMR spectrum showed glucosyl moiety [δ_C 103.2 (C-1'), δ_C 75.0 (C-2'), δ_C 78.1 (C-3'), δ_C 71.7 (C-4'), δ_C 78.4 (C-5'), δ_C 62.7 (C-6')]. With ^1H and ^{13}C NMR spectra, the structure of compound **5** was assigned as 3,4,5- trimethoxyphenol 1-*O*-*β*-D-glucopyranoside. (Xiong et al. 2015)

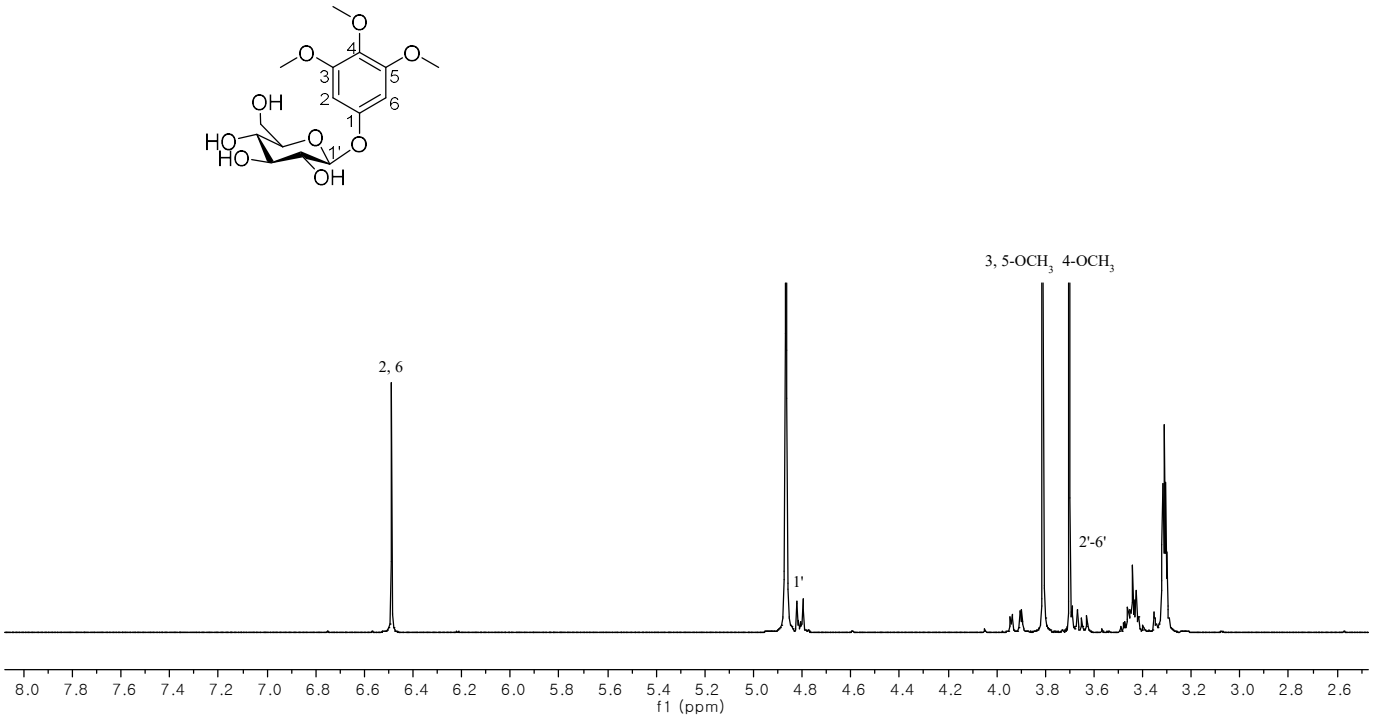


Figure 13. ^{1}H NMR spectrum of compound **5** (300 MHz, CD_3OD)

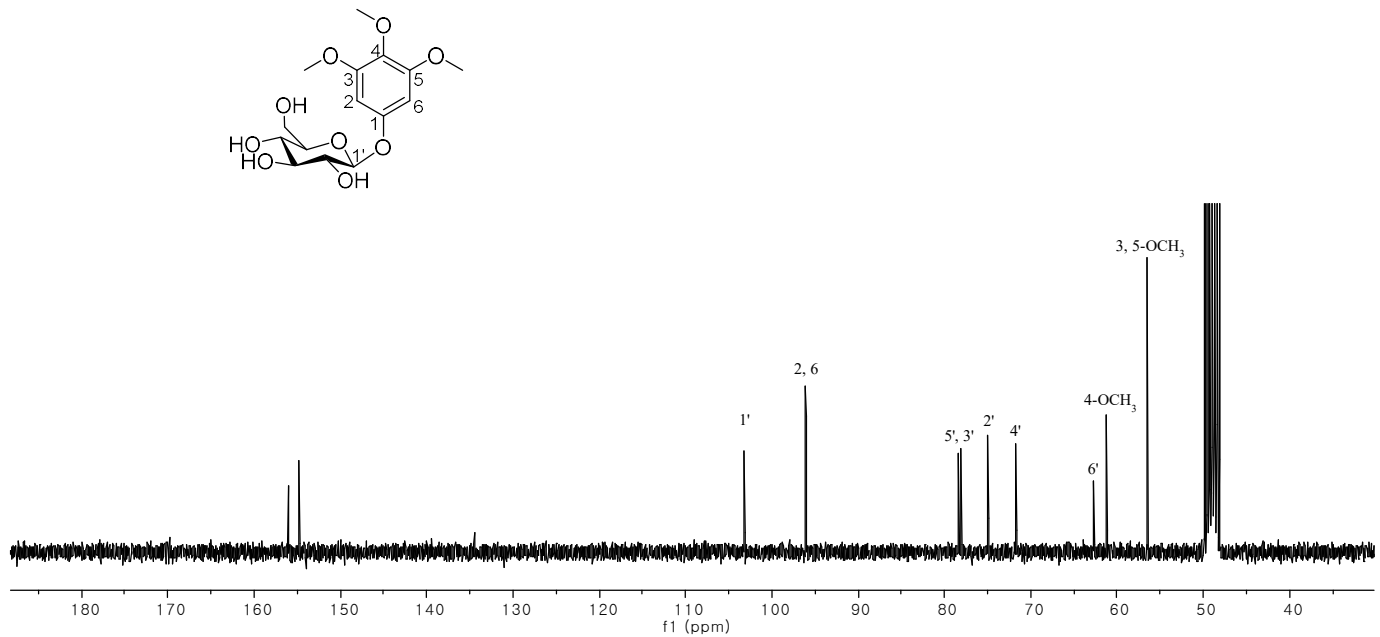


Figure 14. ^{13}C NMR spectrum of compound **5** (75 MHz, CD_3OD)

3.6. Compound 6

Compound **6** was obtained as white amorphous powder with molecular formula $C_{21}H_{24}O_{10}$, based on the *m/z* 435.1292 $[M-H]^-$ in HRMS (ESI-QTOF). The ^1H NMR spectrum of **6** exhibited one 1,4-disubstituted benzene ring [δ_H 7.00 (2H, d, *J* = 8.5Hz, H-2 and H-6), δ_H 6.68 (2H, d, *J* = 8.5Hz, H-3 and H-5),] and another 1,2,3,5-tetrasubstituted benzene ring [δ_H 6.47 (H, d, *J* = 2.1Hz, H-6'), δ_H 6.41 (H, d, *J* = 2.1Hz, H-4')] and four benzylic protons [δ_H 3.16 (2H, m, H-8) and δ_H 2.76 (2H, m, H-7)] which indicated the presence of dihydrostilbenoid. It also showed the signal of an anomeric proton at δ_H 4.86 (1H, d, *J* = 7.4Hz, H-1''). In ^{13}C NMR spectrum, Carbon signal at δ_C 174.5, along with strong IR absorption peak at 1610cm^{-1} indicated carboxylate group. The ^{13}C NMR spectrum also showed glucosyl moiety [δ_C 101.4 (C-1''), δ_C 74.7 (C-2''), δ_C 77.9 (C-3''), δ_C 71.3 (C-4''), δ_C 78.2 (C-5''), δ_C 62.4 (C-6'')]. With ^1H and ^{13}C NMR spectra, the structure of compound **6** was assigned as cudrabibenzyl A. (Hiep et al. 2017)

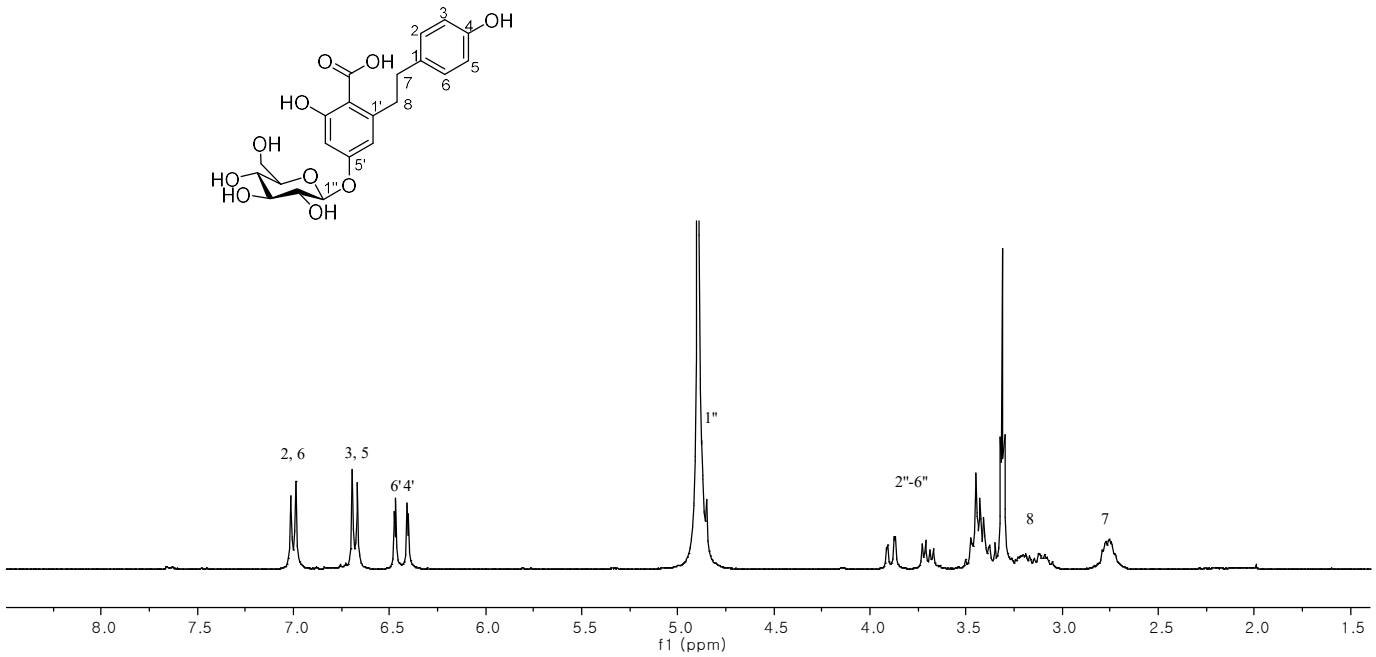


Figure 15. ^{1}H NMR spectrum of compound **6** (300 MHz, CD_3OD)

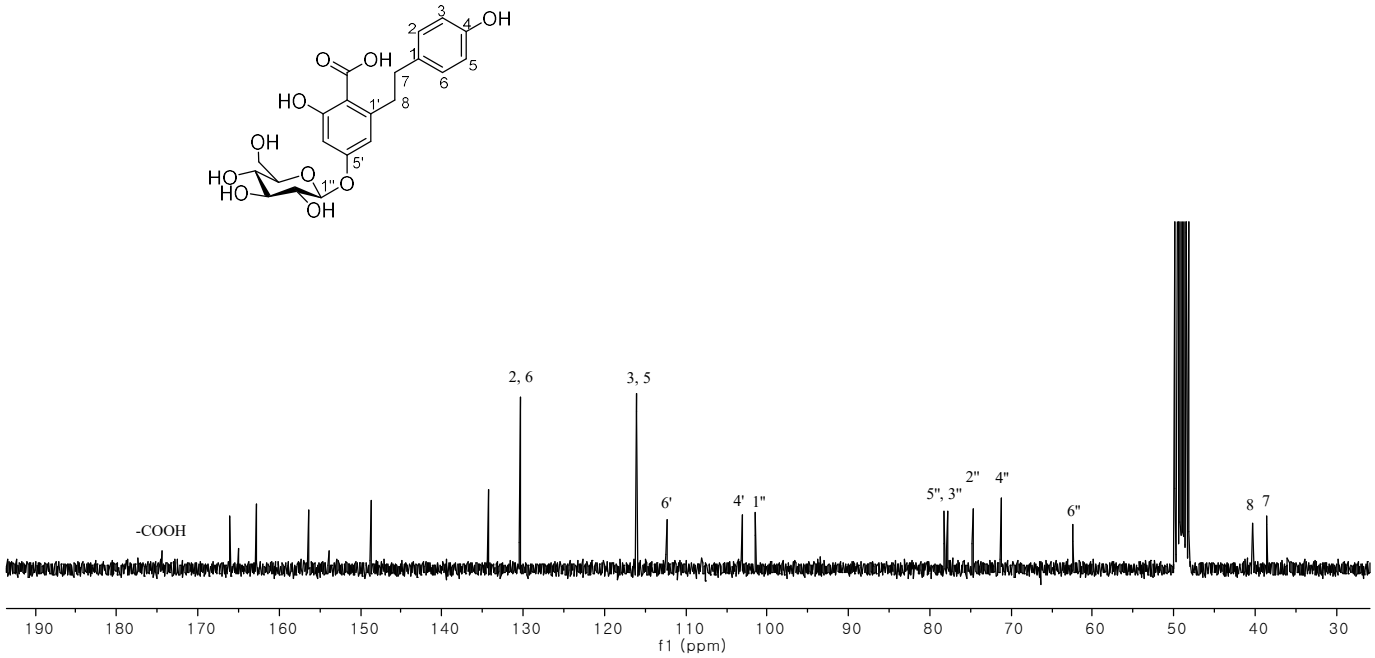


Figure 16. ^{13}C NMR spectrum of compound **6** (75 MHz, CD_3OD)

3.7. Compound 7

Compound **7** was obtained colorless amorphous powder with molecular formula $C_{19}H_{30}O_8$, based on the *m/z* 385.1855 $[M-H]^-$ in HRMS (ESI-QTOF). The ^{13}C NMR spectrum of **7** exhibited *α,β*-unsaturated ketone moiety with the signal of ketone at δ_C 201.1 (C-3), along with strong IR absorption peak at 1652cm^{-1} and signals of olefinic carbons at δ_C 167.1 (C-5) and δ_C 127.1 (C-4). It also exhibited the signals of two olefinic carbons [δ_C 135.2 (C-8), δ_C 131.4 (C-7)], and two oxygenated carbons [δ_C 77.2 (C-9), δ_C 79.9 (C-6)], and one methylene carbon[δ_C 50.6 (C-2)], and four methyl carbon [δ_C 42.4 (C-1), δ_C 24.7 (C-12), δ_C 23.4(C-11), δ_C 21.2 (C-10)]. The ^{13}C NMR spectrum also showed glucosyl moiety [δ_C 102.6 (C-1'), δ_C 75.0 (C-2'), δ_C 77.9 (C-3'), δ_C 71.5 (C-4'), δ_C 78.0 (C-5'), δ_C 62.7 (C-6')]. The ^1H NMR spectrum exhibited the signal of an anomeric proton at δ_H 4.31 (1H, d, J = 7.8Hz, H-1''). With ^1H and ^{13}C NMR spectra, the structure of compound **7** was assigned as roseoside.

The chemical shift of C-9 was δ_C 77.2, indicating (9*R*)-configuration. The configuration of C-6 was identified by optical rotatory power, $[\alpha]_D^{20}$ 34.6 (*c* 0.10, MeOH), indicating (6*S*)-configuration. With all this evidence, compound **7** was assigned as (6*R*, 9*S*)-roseoside. (Mamadalieva et al. 2014)

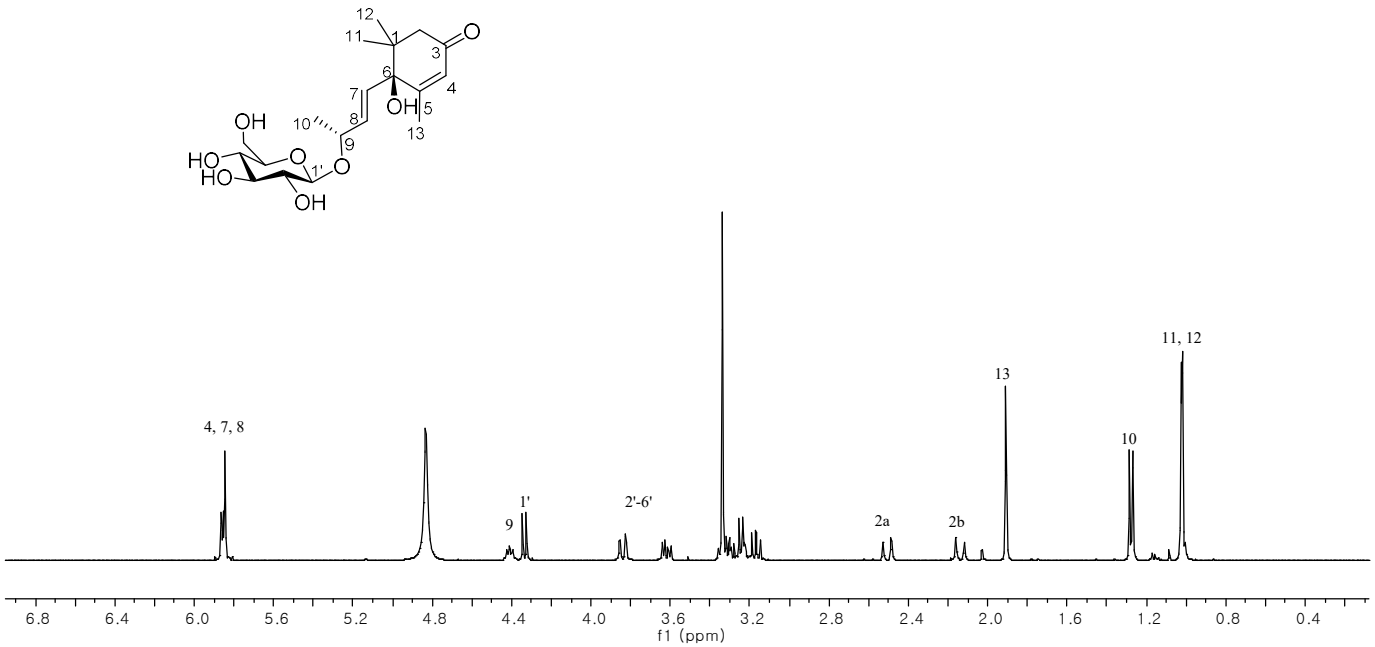


Figure 17. ^{1}H NMR spectrum of compound **7** (300 MHz, CD_3OD)

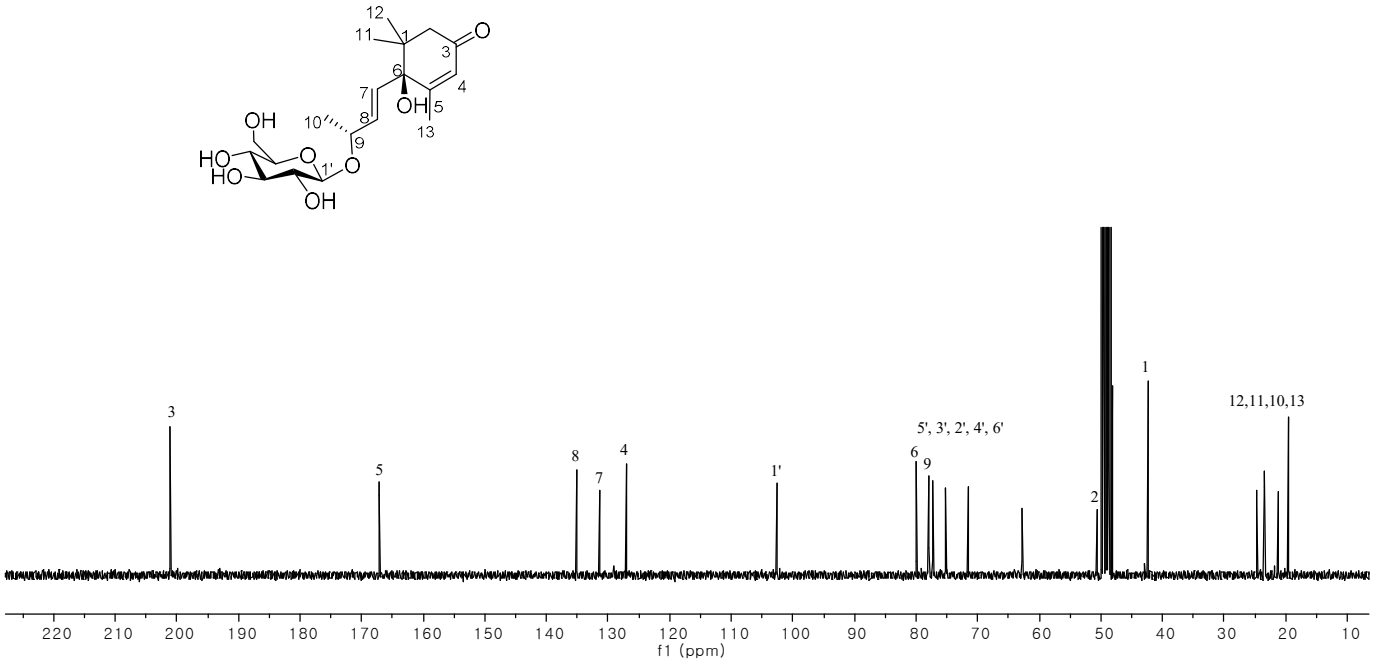


Figure 18. ^{13}C NMR spectrum of compound **7** (75 MHz, CD_3OD)

3.8. Compound 8

Compound **8** was obtained as dark yellow amorphous powder with molecular formula $C_{14}H_{14}O_7$, based on the *m/z* 293.1 $[M-H]^-$ in ESIMS. In the ^1H and ^{13}C NMR spectra, caffeoyl moiety was established, that consists of one 1,3,4-trisubstittuted bemzene ring [δ_H 7.05 (H, d, J = 1.8Hz, H-2'), δ_H 6.96 (H, dd, J = 8.2Hz, 1.8Hz, H-6') and δ_H 6.77 (H, d, J = 8.2Hz, H-5')], one trans-oriendted olefinic group [δ_H 7.62 (H, d, J = 15.9Hz, H-7'), δ_H 7.32 (H, d, J = 15.9Hz, H-8')] and one ester group [δ_C 168.8 (C-9')]. ^{13}C NMR spectrum also showed the signal of another ester at δ_C 180 (C-1), three oxygenated carbons at δ_C 76.9 (C-3), δ_C 74.4 (C-2) and δ_C 71.9 (C-4), and methyl carbon at δ_C 23.2 (C-5). With ^1H and ^{13}C NMR spectra, the structure of compound **8** was assigned as 3-*O*-caffeoyl-2-*C*-methyl-*D*-erythrono-1,4-lactone. (Ogawa et al. 1992)

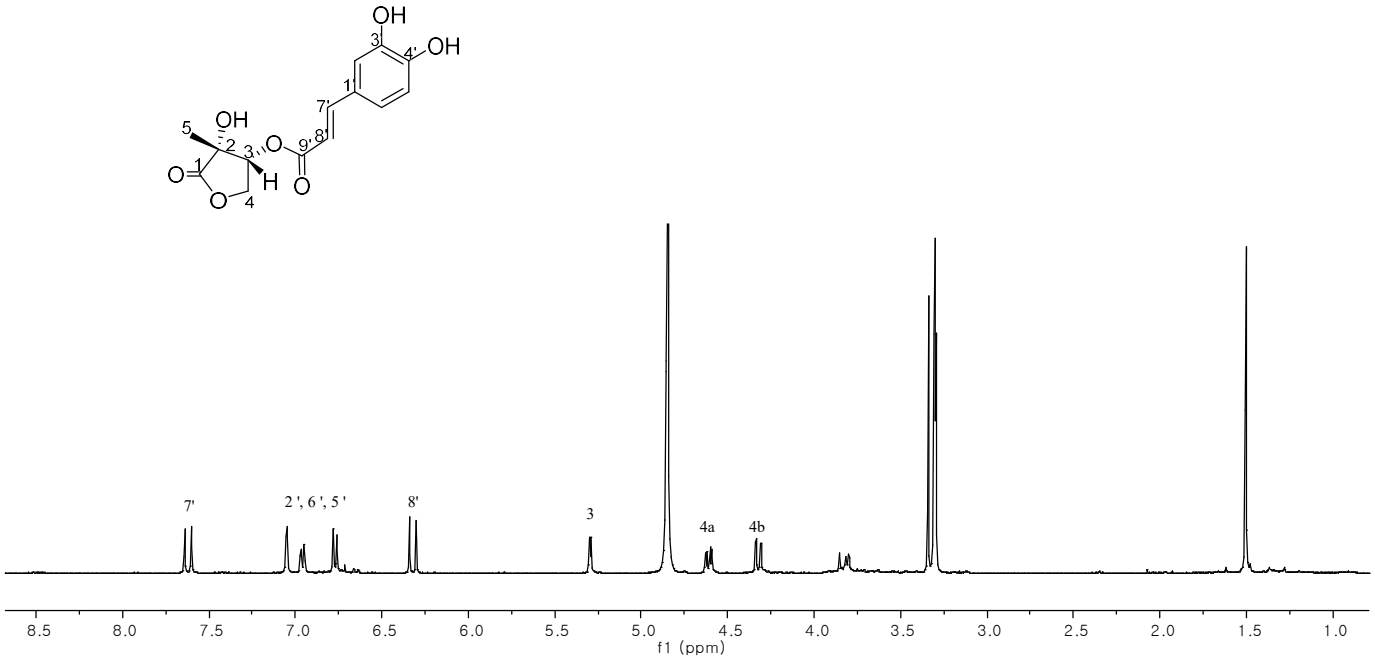


Figure 19. ^{1}H NMR spectrum of compound **8** (300 MHz, CD_3OD)

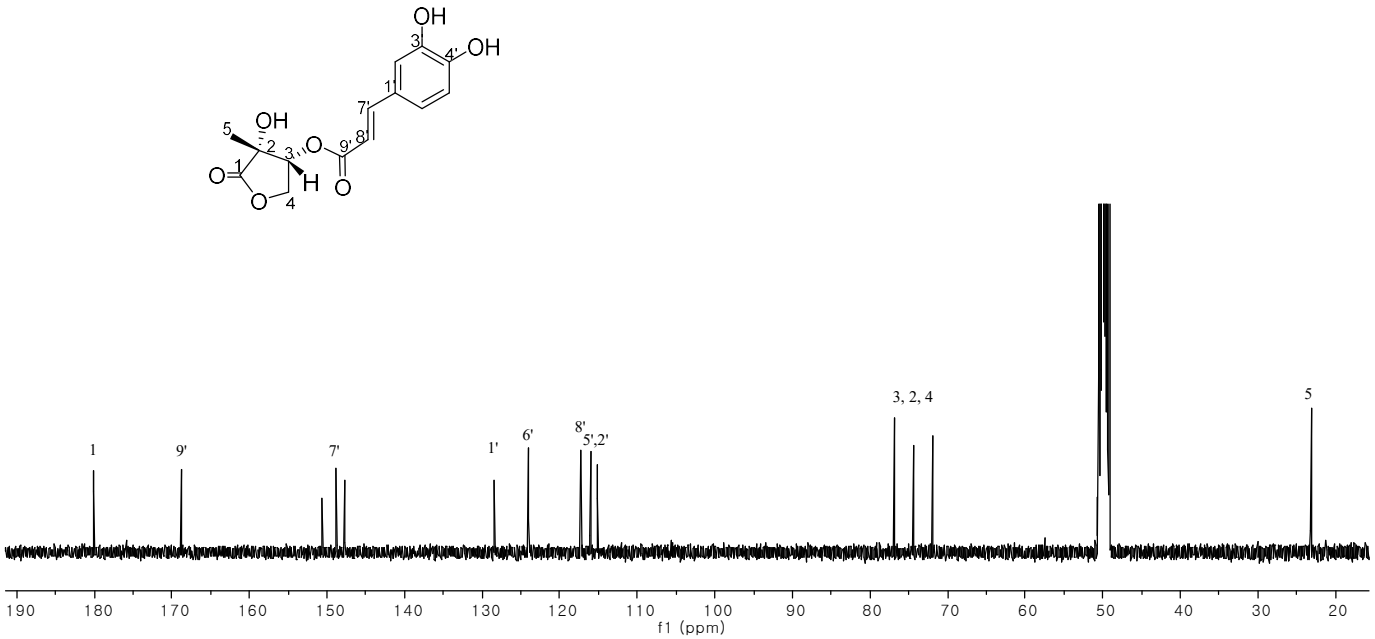


Figure 20. ^{13}C NMR spectrum of compound **8** (75 MHz, CD_3OD)

3.9. Compound 9

Compound **9** was obtained as colorless amorphous powder with molecular formula $C_{16}H_{18}O_9$, based on the *m/z* 353.1 $[M-H]^-$ in ESIMS. In the ^1H and ^{13}C NMR spectra, caffeoyl moiety was established, compared to ^1H and ^{13}C NMR spectra of **8**. ^{13}C NMR spectrum exhibited quinic acid moiety with the signal of carboxylic acid group at δ_C 177.0 (-COOH), four oxygenated carbons at δ_C 73.5 (C-1), δ_C 72.0 (C-3), δ_C 72.0 (C-4) and δ_C 71.3 (C-5), and two methylene carbon at δ_C 38.7 (C-6) and δ_C 38.2 (C-2). With ^1H and ^{13}C NMR spectra, the structure of compound **9** was assigned as chlorogenic acid. (Zhao et al. 2014)

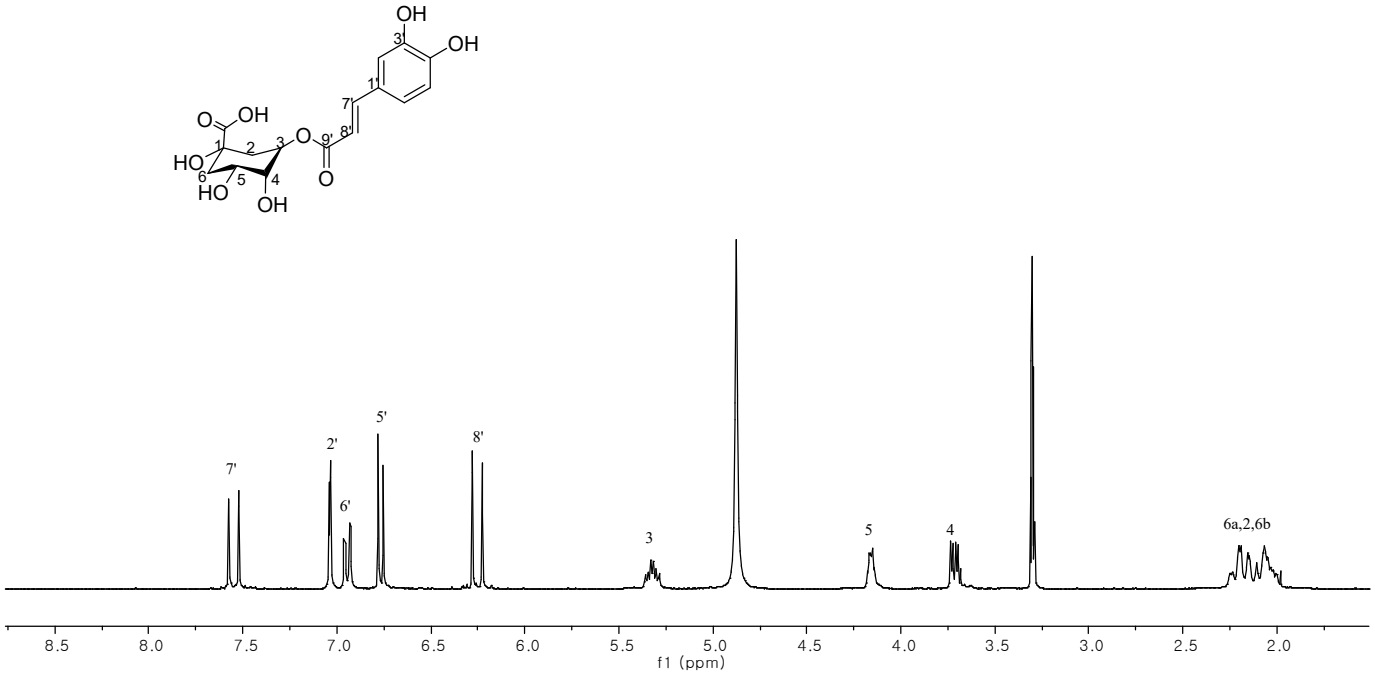


Figure 21. ^{1}H NMR spectrum of compound **9** (300 MHz, CD_3OD)

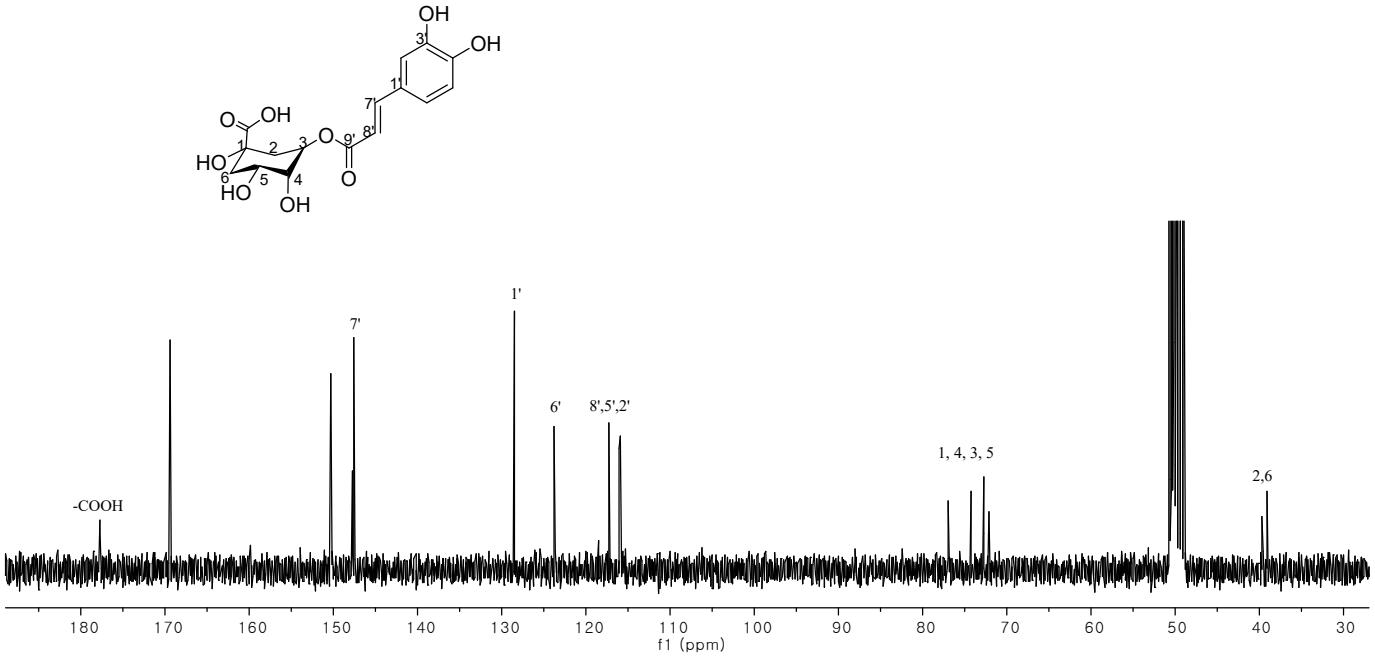


Figure 22. ^{13}C NMR spectrum of compound **9** (75 MHz, CD_3OD)

3.10. Compounds 10-11

Compound **10** was obtained as white amorphous powder with molecular formula $C_9H_6O_3$, based on the *m/z* 161.1 $[M-H]^-$ in ESIMS. Based on ^1H NMR spectrum, 7-hydroxycoumarin moiety was established, [δ_H 7.85 (1H, d, J = 9.5 Hz, H-4), δ_H 7.45 (1H, d, J = 8.5 Hz, H-5), δ_H 6.79 (1H, dd, J = 8.5, 2.3 Hz, H-6), δ_H 6.71 (1H, d, J = 2.3 Hz, H-8), δ_H 6.17 (1H, d, J = 9.5 Hz, H-3)]. With ^1H and ^{13}C NMR spectra, the structure of compound **10** was assigned as umbelliferone. (de Sá de Sousa Nogueira et al. 2013)

Compound **11** was obtained as white amorphous powder with molecular formula $C_{15}H_{16}O_8$, based on the *m/z* 347.2 $[M+Na]^+$ in ESIMS. The ^1H NMR spectrum of **11** was similar to that of **10**, except an anomeric proton signal at δ_H 5.03 (1H, d, J=7.8Hz, H-1'). The ^{13}C NMR spectrum showed glucosyl moiety [δ_C 102.9 (C-1'), δ_C 74.8 (C-2'), δ_C 77.9 (C-3'), δ_C 71.2 (C-4'), δ_C 78.3 (C-5'), δ_C 62.5 (C-6')]. With ^1H and ^{13}C NMR spectra, the structure of compound **11** was assigned as skimmin. (Sun et al. 2016)

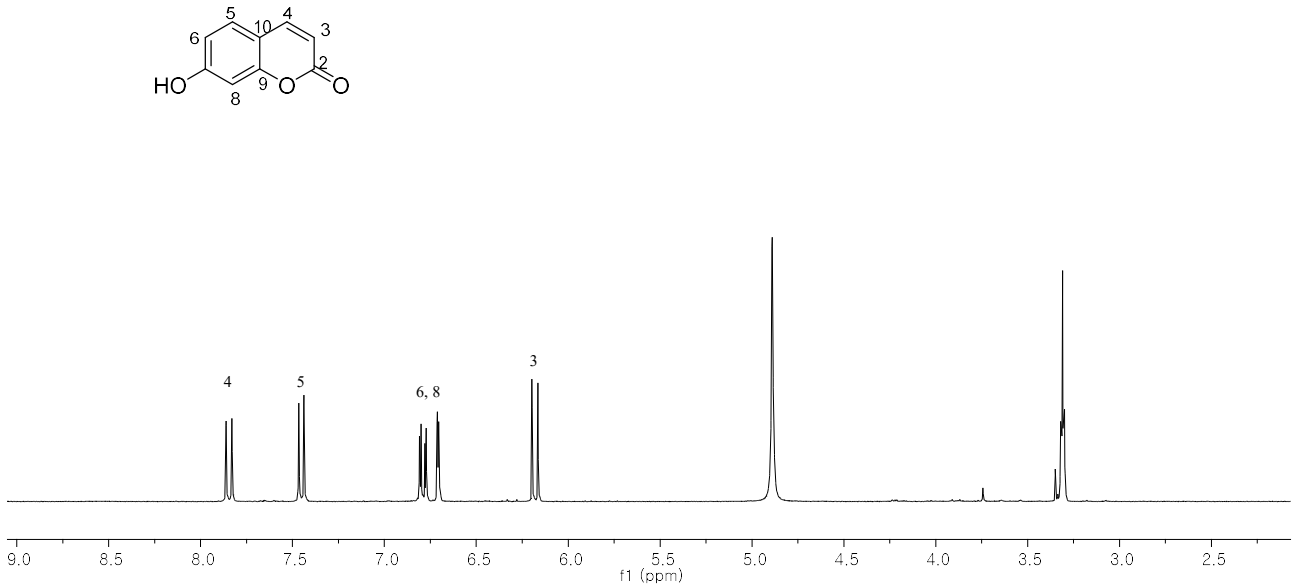


Figure 23. ^{1}H NMR spectrum of compound **10** (300 MHz, CD_3OD)

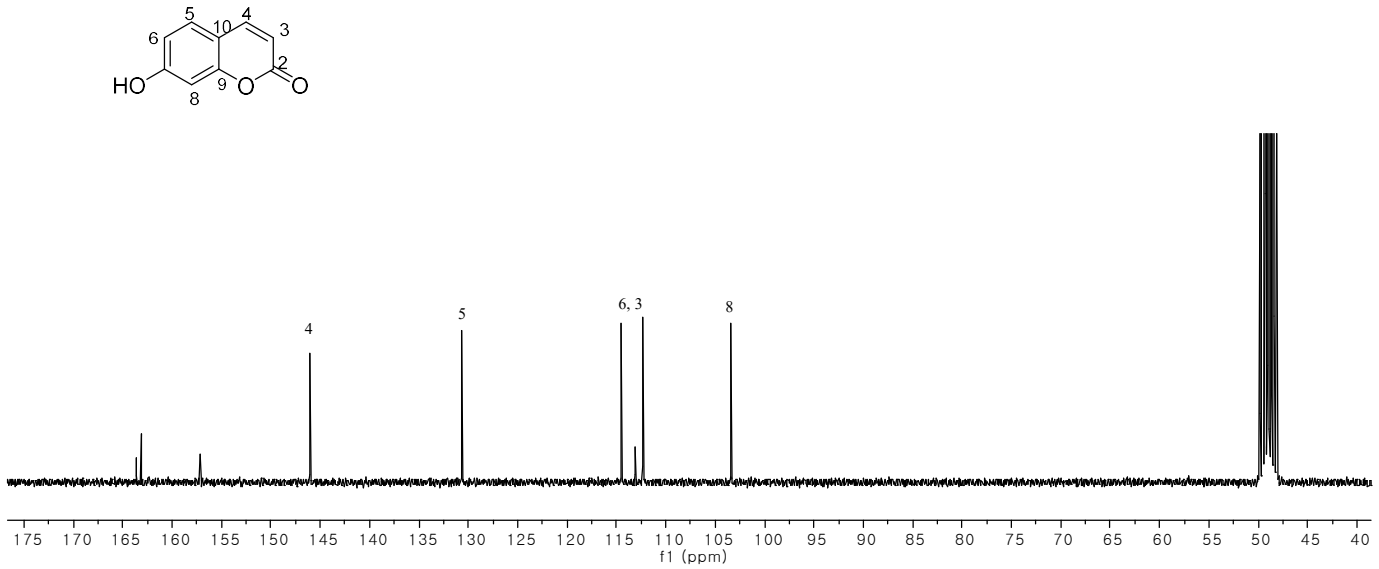


Figure 24. ^{13}C NMR spectrum of compound **10** (75 MHz, CD_3OD)

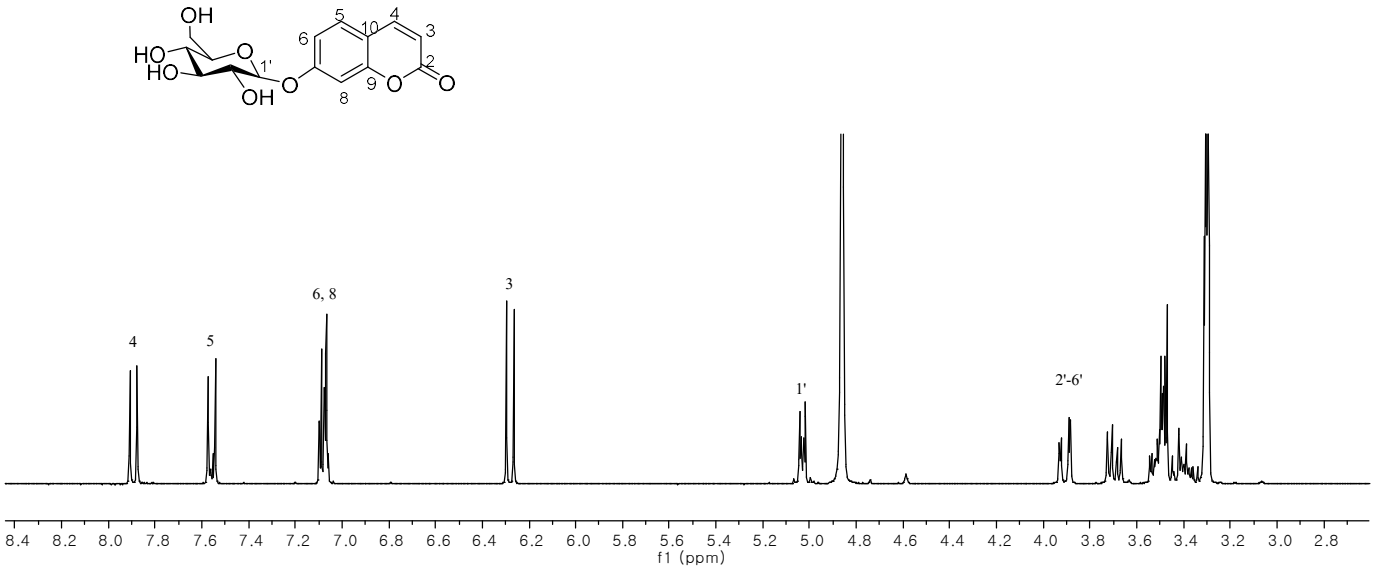


Figure 25. ^{1}H NMR spectrum of compound **11** (300 MHz, CD_3OD)

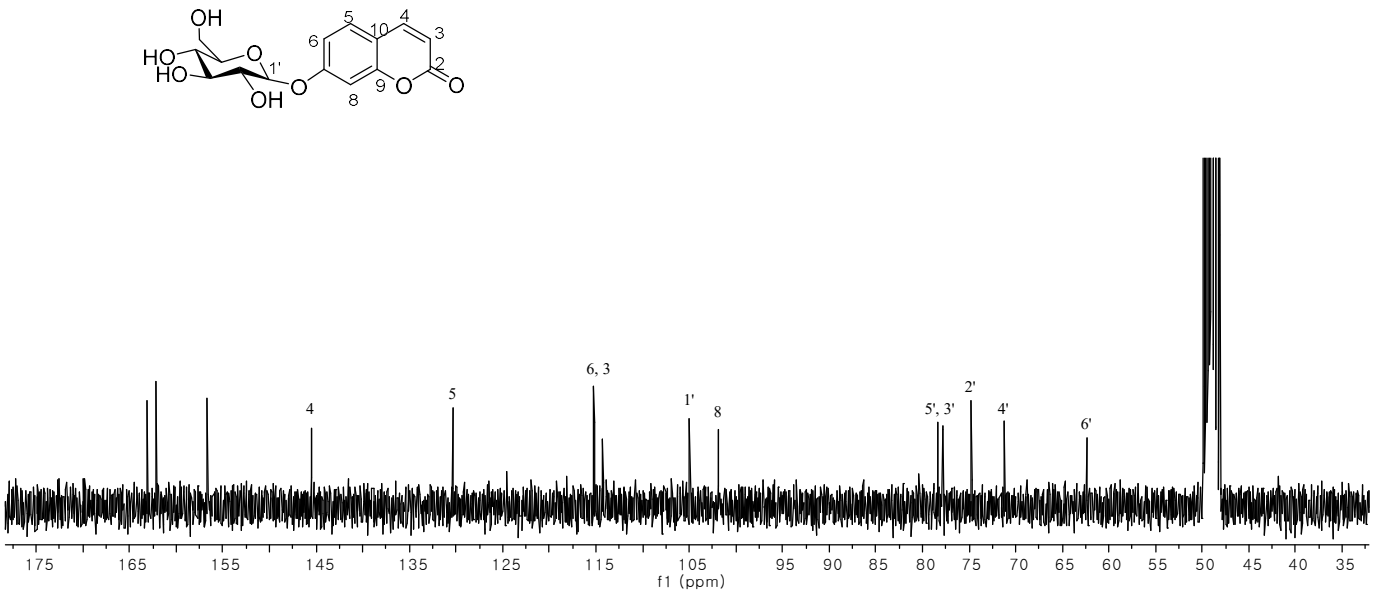


Figure 26. ^{13}C NMR spectrum of compound **11** (75 MHz, CD_3OD)

3.11. Compound 12

Compound **12** was obtained as white amorphous powder with molecular formula $C_{15}H_{16}O_9$, based on the *m/z* 339.1 $[M-H]^-$ in ESIMS. Based on ^1H NMR spectrum, 6,7-dihydroxycoumarin moiety was established [δ_H 7.84 (1H, d, J = 9.4 Hz, H-4), 7.47 (1H, s, H-5), 6.79 (1H, s, H-8), 6.21 (1H, d, J = 9.4 Hz, H-3)]. ^1H NMR spectrum showed the signal of an anomeric proton at δ_H 4.85 (1H, d, J = 7.4Hz, H-1'). The ^{13}C NMR spectrum also showed glucosyl moiety [δ_C 104.2 (C-1'), δ_C 74.8 (C-2'), δ_C 77.4 (C-3'), δ_C 71.3 (C-4'), δ_C 78.5 (C-5'), δ_C 62.5 (C-6')]. With ^1H and ^{13}C NMR spectra, the structure of compound **12** was assigned as esculin. (Bayoumi et al. 2010)

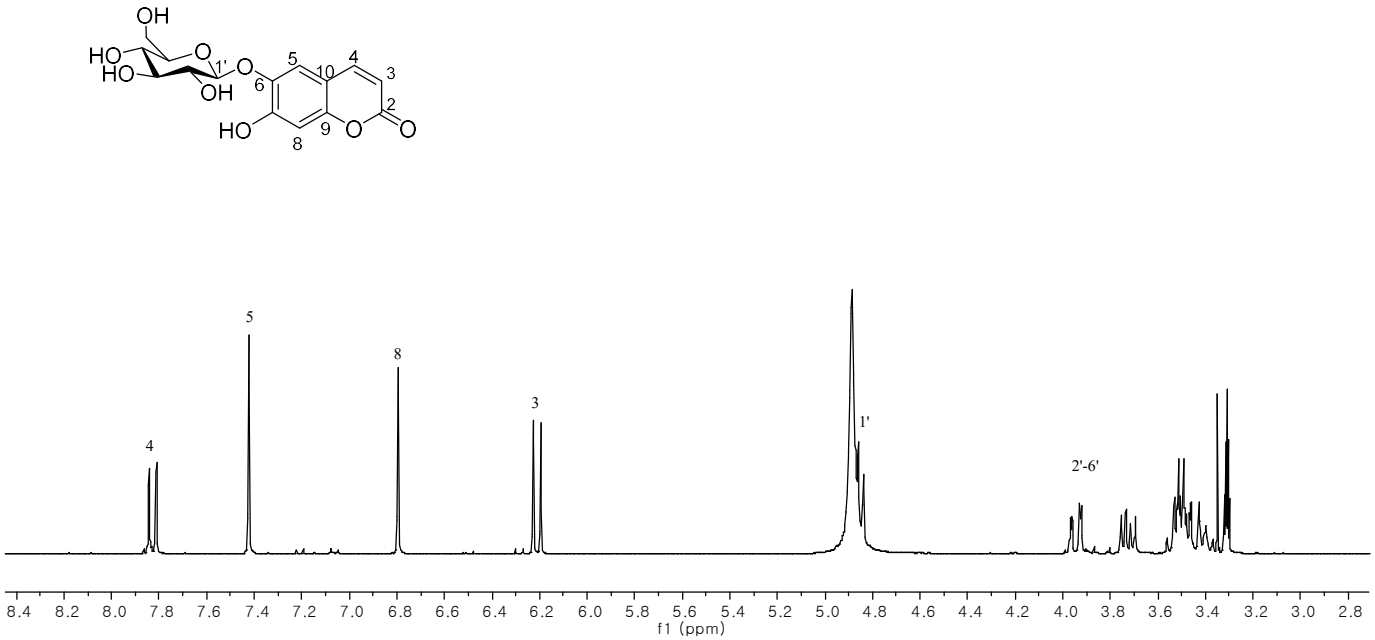


Figure 27. ^{1}H NMR spectrum of compound **12** (300 MHz, CD_3OD)

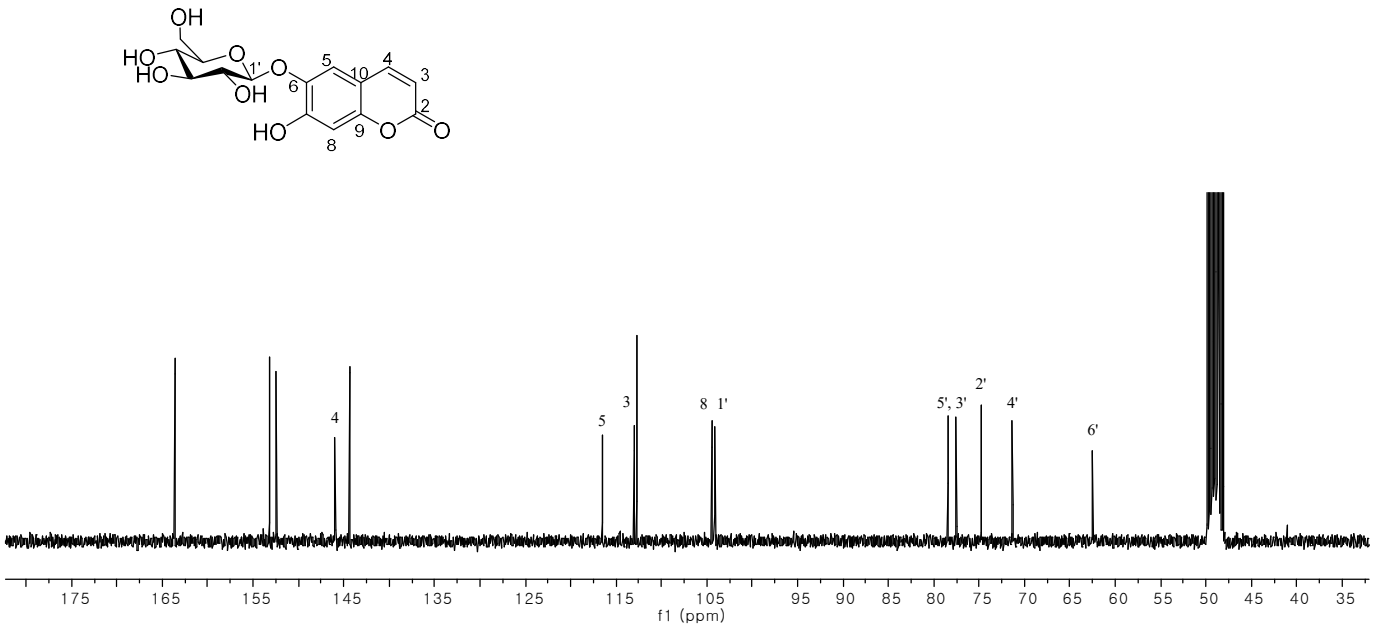


Figure 28. ^{13}C NMR spectrum of compound **12** (75 MHz, CD_3OD)

3.12. Compound 13

Compound **13** was obtained as pale yellow amorphous powder with molecular formula $C_{10}H_{12}O_5$, based on the m/z 211.0598 $[M-H]^-$ in ESIMS. The ^1H NMR spectrum of **13** exhibited 1,3,4-trisubstituted benzene ring, whose signals were observed at δ_H 7.60 (1H, m, H-6'), δ_H 7.57 (1H, brs, H-2') and δ_H 6.88 (1H, d, J = 8.5Hz, H-5'). It also exhibited the presence of one methoxy group [δ_H 3.91 (3H, s, 3'-OCH_3)]. The ^{13}C NMR spectrum showed the signal of ketone at δ_C 199.5 (C-1) and two oxygenated carbon at δ_C 75.5 (C-2) and δ_C 66.3 (C-3). With ^1H and ^{13}C NMR spectra, the structure of compound **13** was assigned as *C*-veratroylglycol. (Baderschneider et al. 2001)

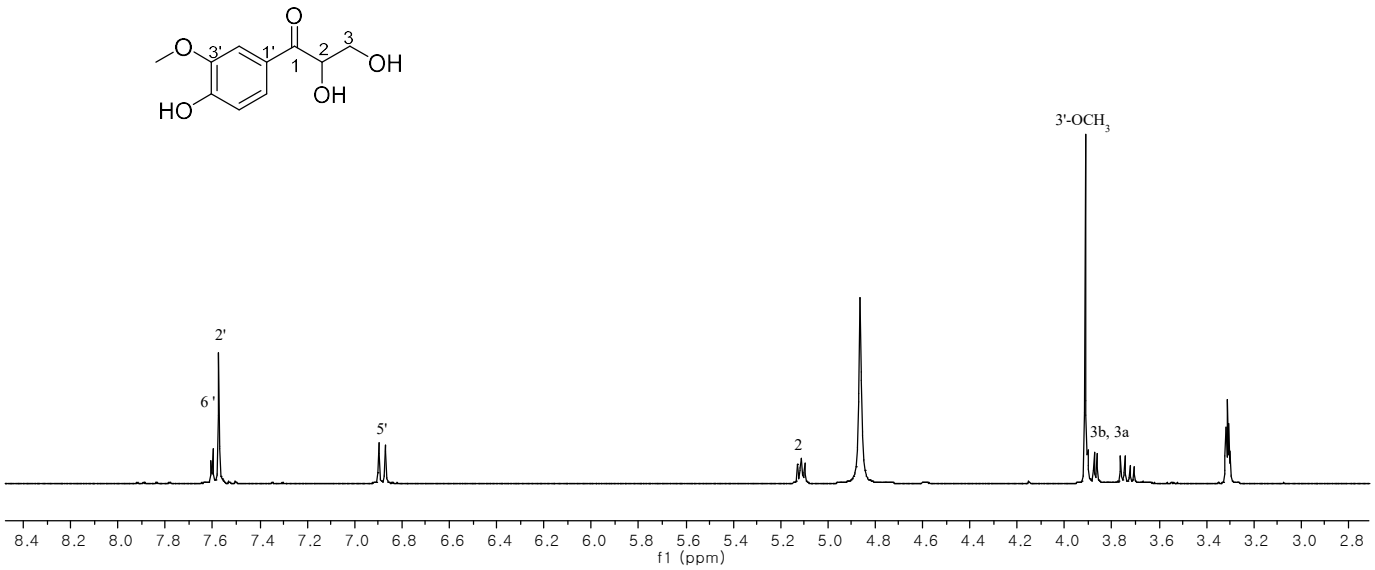


Figure 29. ^{1}H NMR spectrum of compound **13** (300 MHz, CD_3OD)

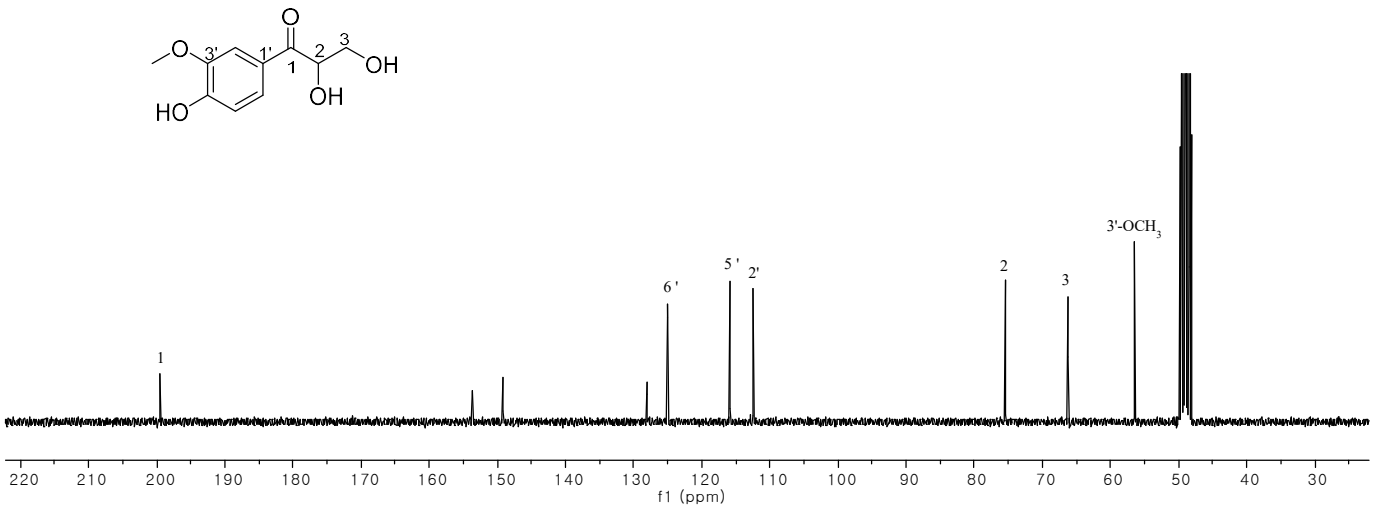


Figure 30. ^{13}C NMR spectrum of compound **13** (75 MHz, CD_3OD)

3.13. Compound 14

Compound **14** was obtained as pale yellow amorphous powder with molecular formula $C_{11}H_{14}O_6$, based on the m/z 241.1 $[M-H]^-$ in ESIMS. The ^1H NMR spectrum of **14** exhibited 1,3,4,5-tetrasubstituted benzene ring, whose signals were observed at δ_H 7.34 (2H, s, H-2' and H-6'). It also exhibited the presence of two methoxy groups [δ_H 3.90 (6H, s, 3', 5'-OCH_3)]. The ^{13}C NMR spectrum showed the signal of ketone group at δ_C 199.6 (C-1) and two oxygenated carbon at δ_C 75.6 (C-2) and δ_C 66.3 (C-3). With ^1H and ^{13}C NMR spectra, the structure of compound **14** was assigned as 2,3-dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)propan-1-one. (Lee et al. 2002)

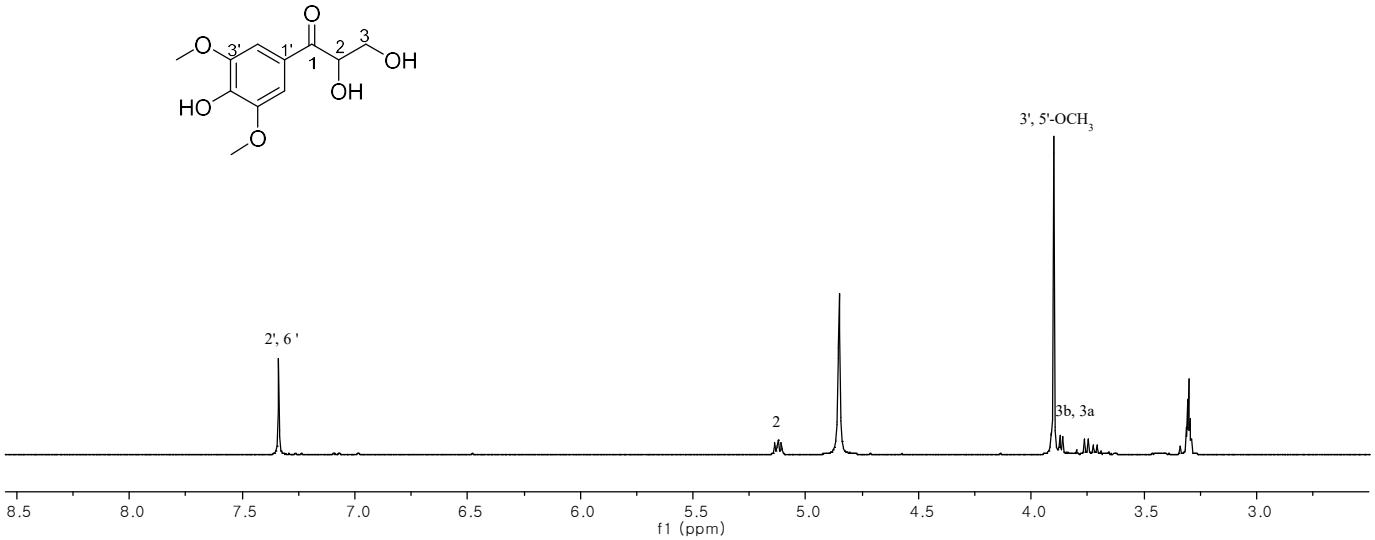


Figure 31. ^{1}H NMR spectrum of compound **14** (300 MHz, CD_3OD)

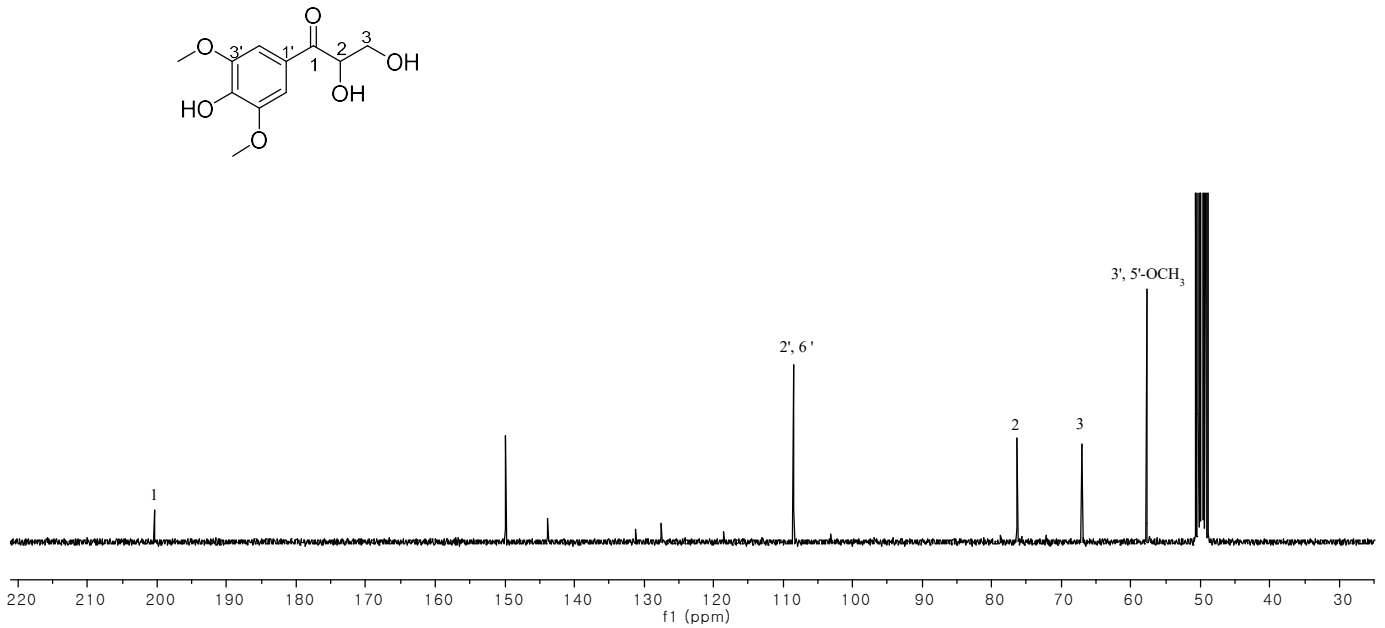


Figure 32. ^{13}C NMR spectrum of compound **14** (75 MHz, CD_3OD)

3.14. Compounds 15-16

Compound **15** was obtained as white amorphous powder with molecular formula $C_7H_6O_3$, based on the *m/z* 137.1 $[M-H]^-$ in ESIMS. The ^1H NMR spectrum of **15** exhibited 1,4-disubstituted benzene ring, whose signals were observed at δ_H 7.86 (2H, d, J = 8.8Hz, H-2, 6) and δ_H 6.80 (2H, d, J = 8.8Hz, H-3, 5). The ^{13}C NMR spectrum showed the signal of carboxylic acid group at δ_C 170.2 (C-7). With ^1H and ^{13}C NMR spectra, the structure of compound **15** was assigned 4-hydroxy benzoic acid. (Yuan et al. 2017)

Compound **16** was obtained as white amorphous powder with molecular formula $C_8H_8O_3$, based on the *m/z* 151.1 $[M-H]^-$ in ESIMS. The ^1H NMR spectrum of **16** was similar to that of **15**, except one methoxy group signal at δ_H 3.87 (3H, s, H-1'). With ^1H and ^{13}C NMR spectra, the structure of compound **16** was assigned as methyl-4-hydroxy benzoic acid. (Li et al. 2012)

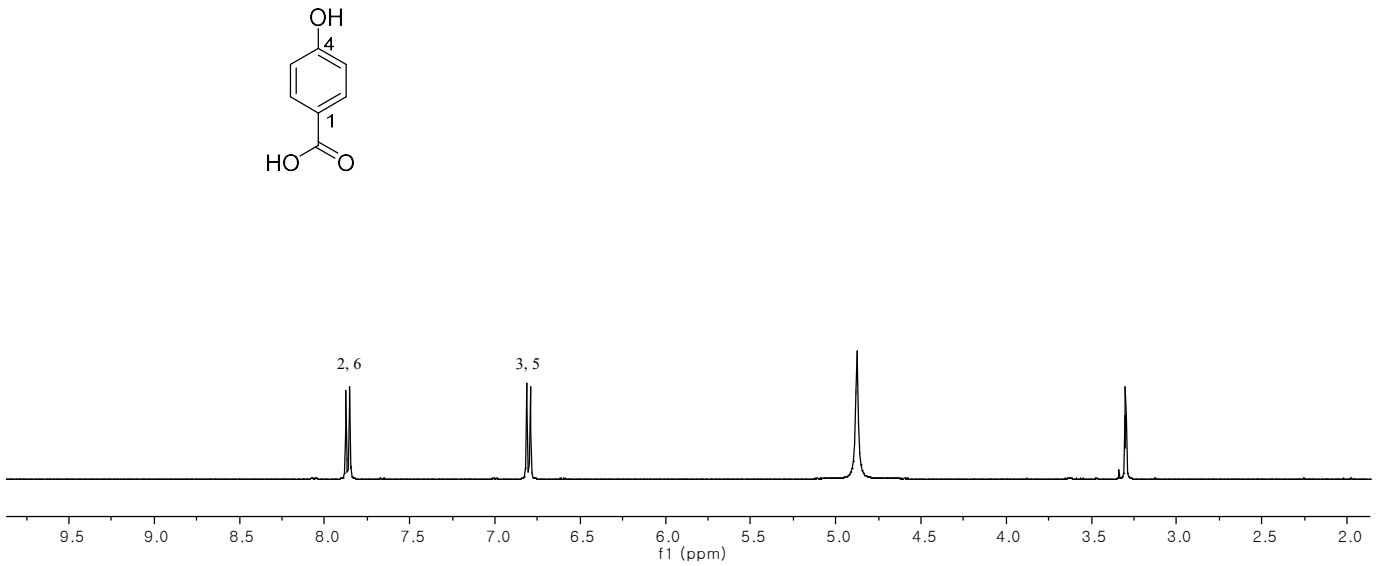


Figure 33. ^{1}H NMR spectrum of compound **15** (300 MHz, CD_3OD)

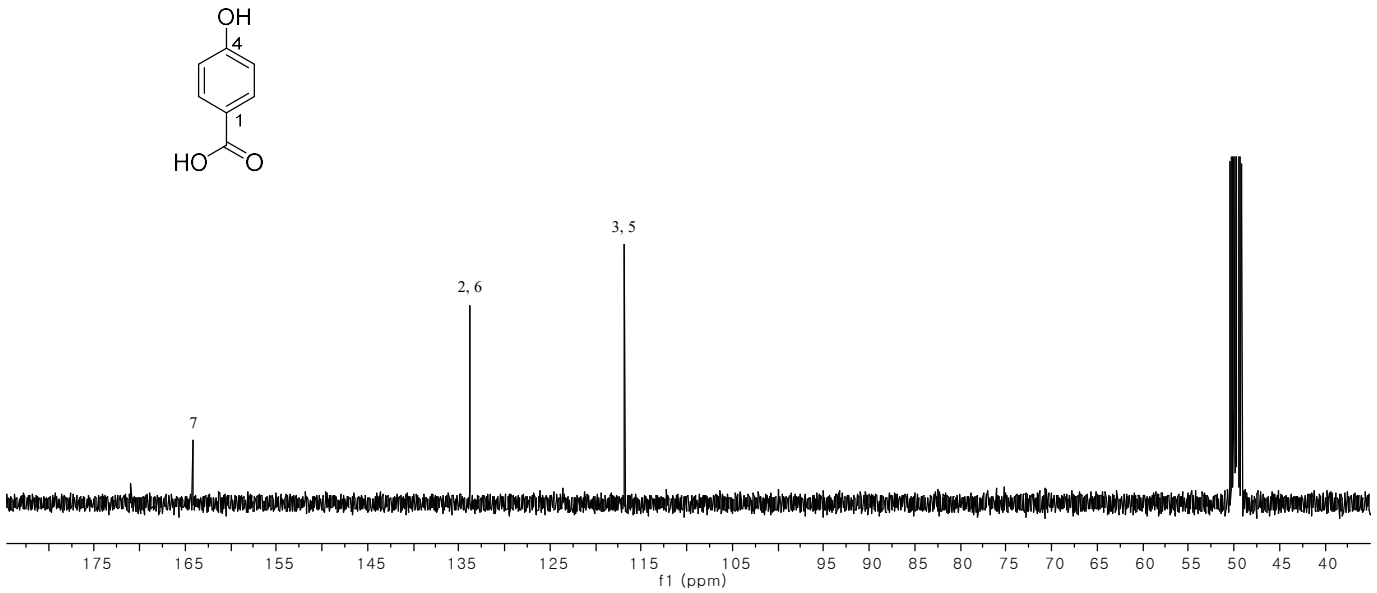


Figure 34. ^{13}C NMR spectrum of compound **15** (75 MHz, CD_3OD)

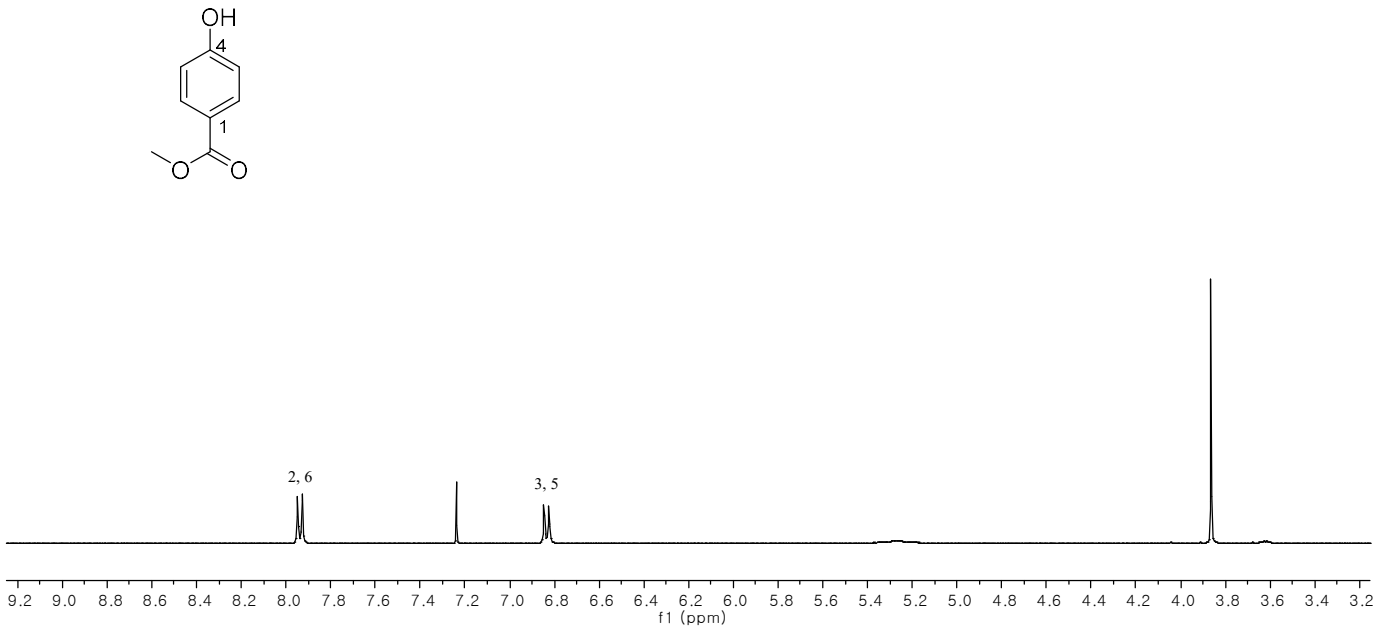


Figure 35. ^{1}H NMR spectrum of compound **16** (300 MHz, $CDCl_3$)

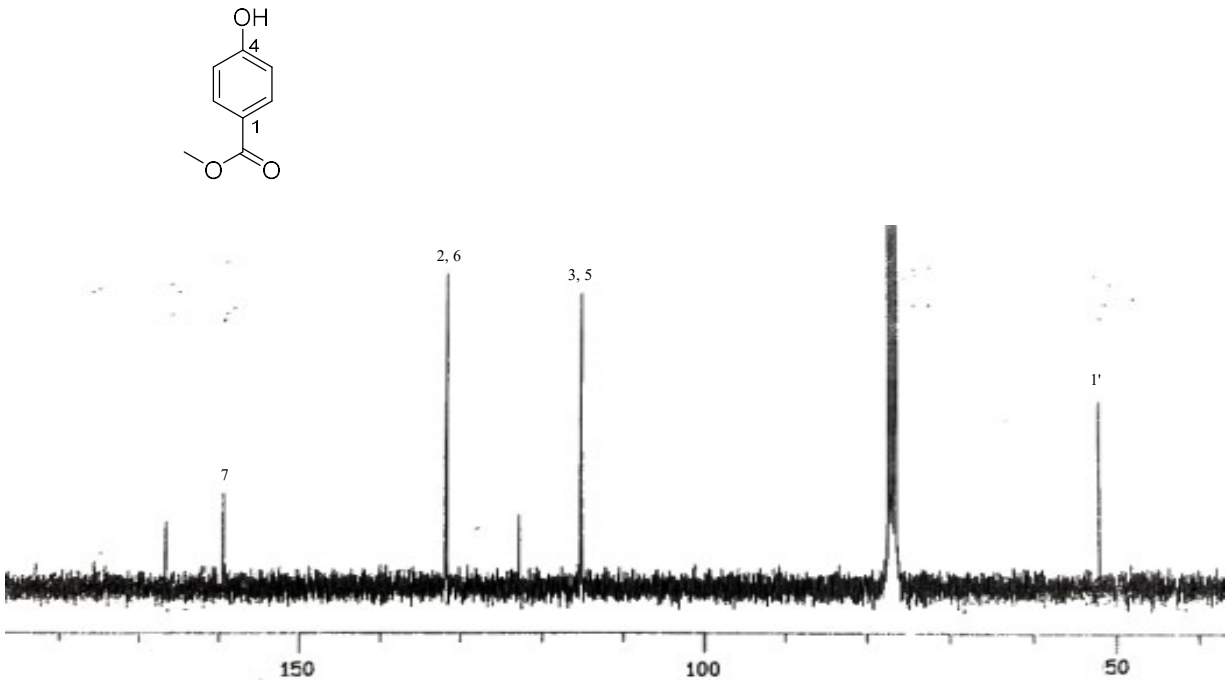


Figure 36. ^{13}C NMR spectrum of compound **16** (75 MHz, $CDCl_3$)

3.15. Compounds 17-19

Compound **17** was obtained as dark yellow amorphous powder with molecular formula $C_{15}H_{10}O_7$, based on the *m/z* 301.0 $[M-H]^-$ in ESIMS. Based on ^1H NMR spectrum, flavonol moiety was established [two meta-coupled aromatic protons at δ_H 6.40 (1H, brs, H-8) and δ_H 6.18 (1H, brs, H-6), 1,3,4-trisubstituted benzene ring at δ_H 7.67 (1H, brs, H-2'), δ_H 7.54 (1H, d, J = 8.4 Hz, H-6') and δ_H 6.87 (1H, m, H-5')]. With ^1H and ^{13}C NMR spectra, the structure of compound **17** was assigned as quercetin. (Wu et al. 2008)

Compound **18** was obtained as yellow amorphous powder with molecular formula $C_{21}H_{20}O_{12}$, based on the *m/z* 463.1 $[M-H]^-$ in ESIMS. The ^1H NMR spectrum of **18** was similar to that of **17**, except an anomeric proton signal at δ_H 5.42 (1H, d, J = 7.4Hz, H-1') and glucosyl moiety [δ_C 100.8 (C-1"), δ_C 74.1 (C-2"), δ_C 76.5 (C-3"), δ_C 69.9 (C-4"), δ_C 77.6 (C-5"), δ_C 61.0 (C-6")]. With ^1H and ^{13}C NMR spectra, the structure of compound **18** was assigned as quercetin-3-*O*-*β*-D-glucopyranoside. (Rajendran et al. 2016)

Compound **19** was obtained as yellow amorphous powder with molecular formula $C_{21}H_{20}O_{12}$, based on the *m/z* 463.1 $[M-H]^-$ in ESIMS. The ^1H NMR spectrum of **19** was similar to that of **17**, except an anomeric proton signal at δ_H 5.08 (1H, d, J = 7.4Hz, H-1") and glucosyl moiety [δ_C 99.8 (C-1"), δ_C 73.1 (C-2"), δ_C 76.4 (C-3"), δ_C 69.5 (C-4"), δ_C 77.1 (C-5"), δ_C 60.6 (C-6")]. With ^1H and ^{13}C NMR spectra, the structure of compound **19** was assigned as quercetin-7-*O*-*β*-D-glucopyranoside. (Wu et al. 2008)

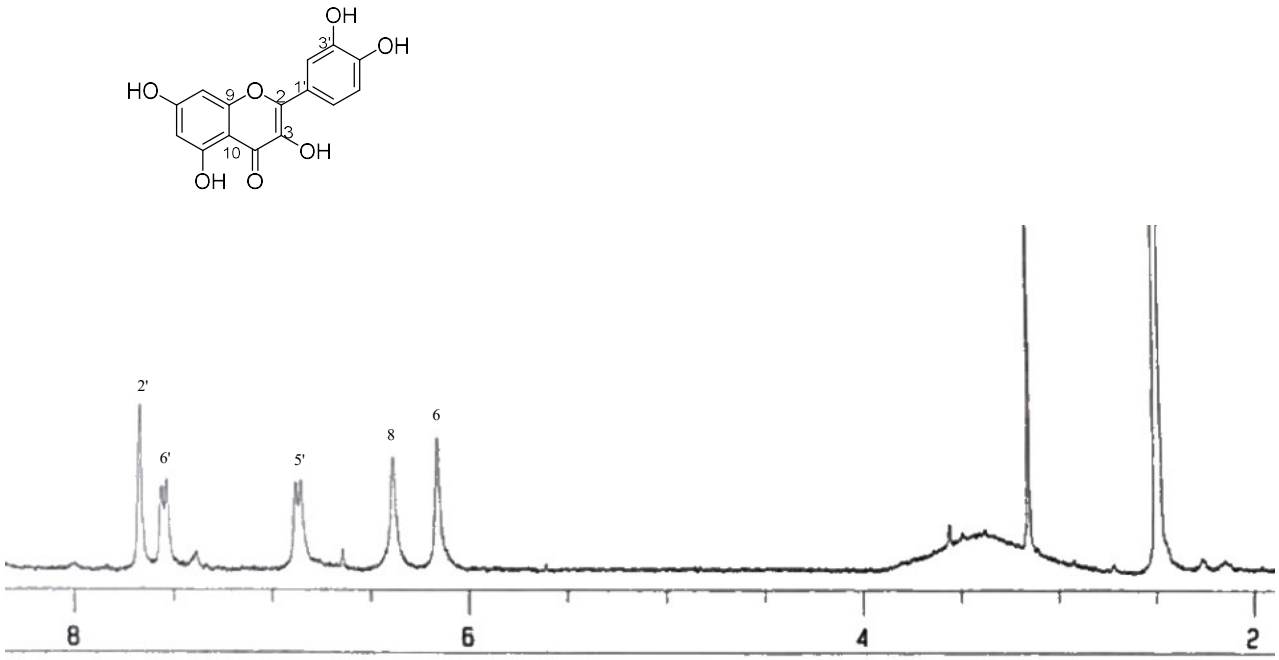


Figure 37. ^{1}H NMR spectrum of compound **17** (300 MHz, DMSO-d_6)

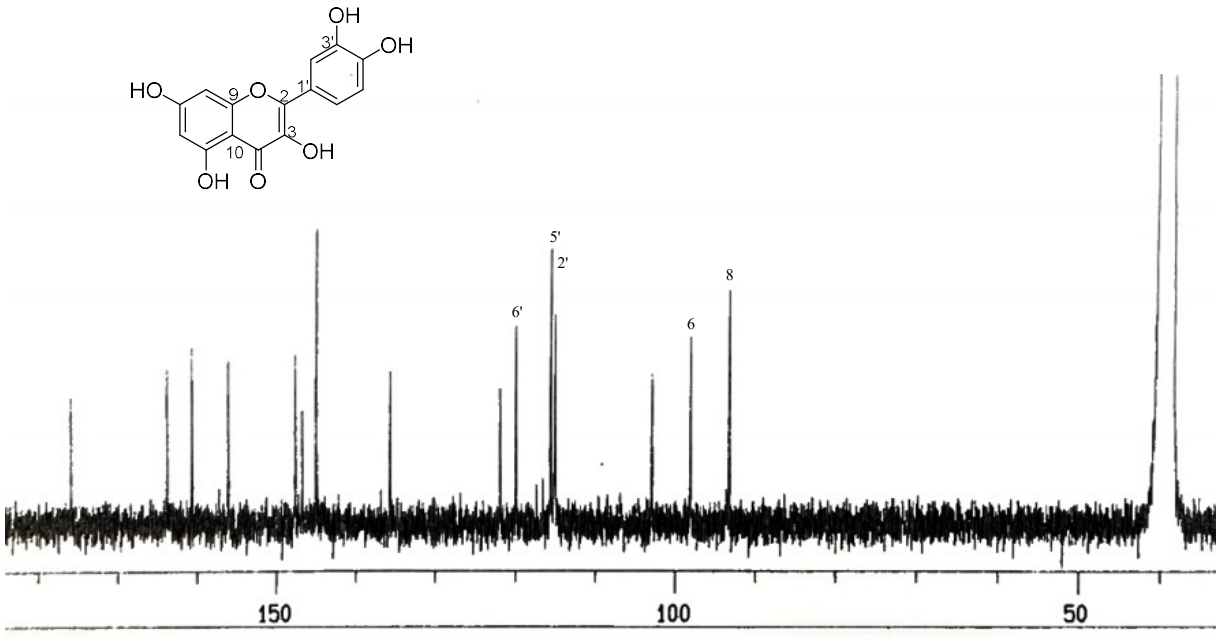


Figure 38. ^{13}C NMR spectrum of compound **17** (75 MHz, DMSO-d_6)

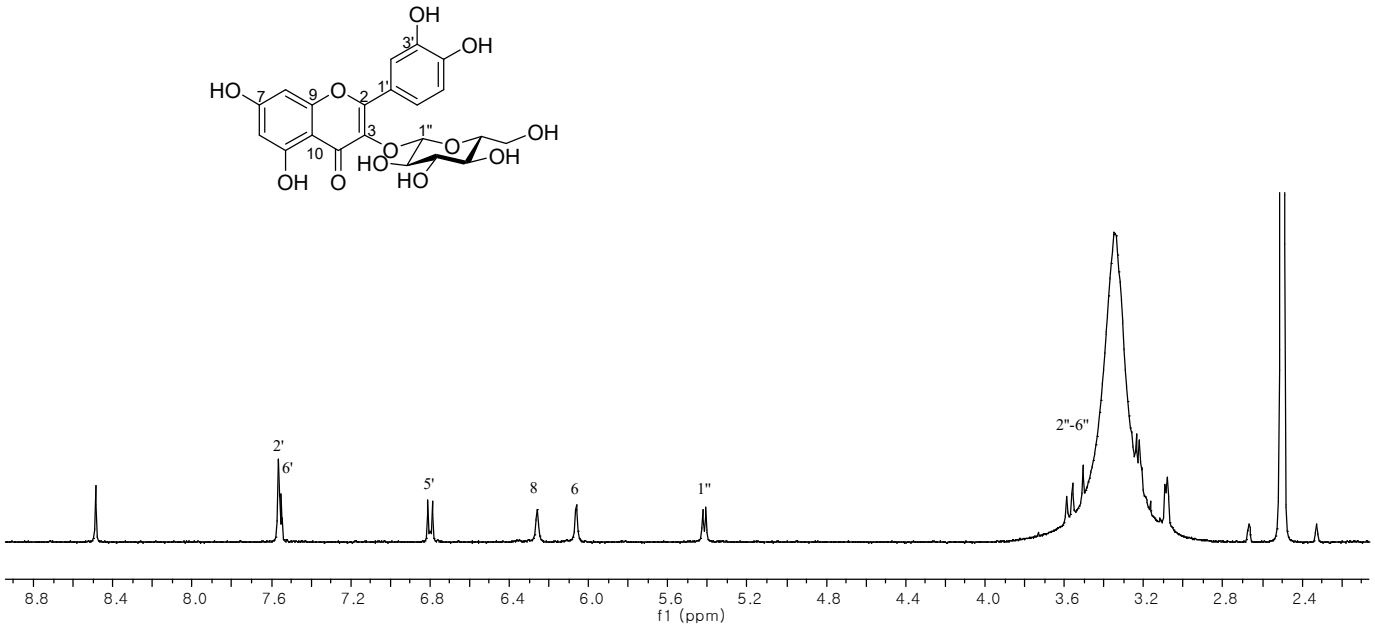


Figure 39. ^{1}H NMR spectrum of compound **18** (300 MHz, DMSO-d_6)

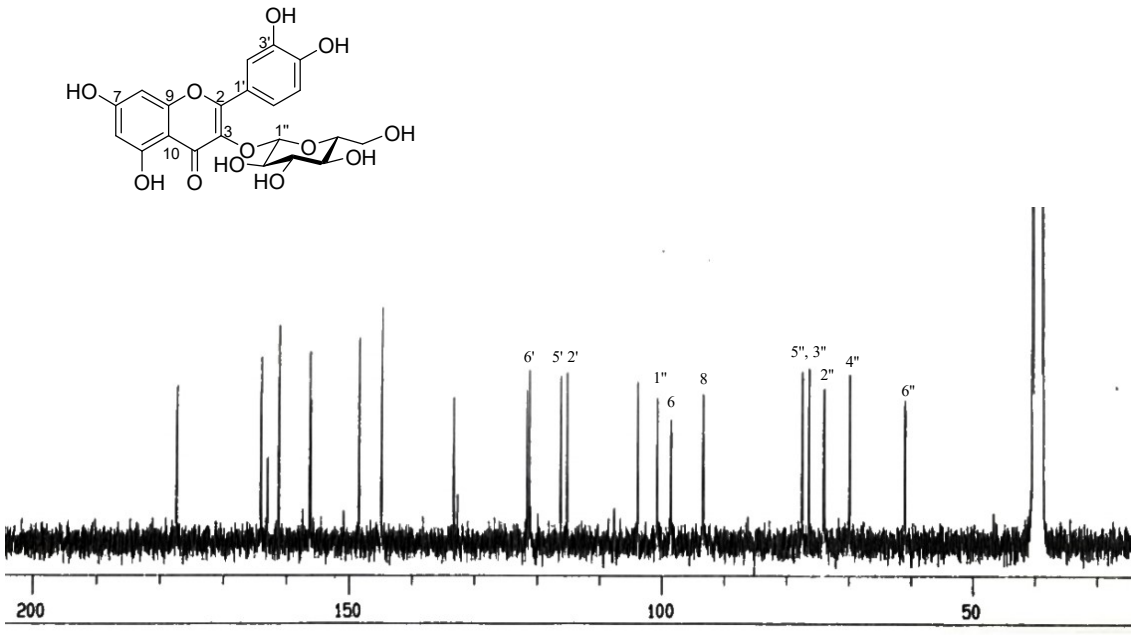


Figure 40. ^{13}C NMR spectrum of compound **18** (75 MHz, DMSO-d_6)

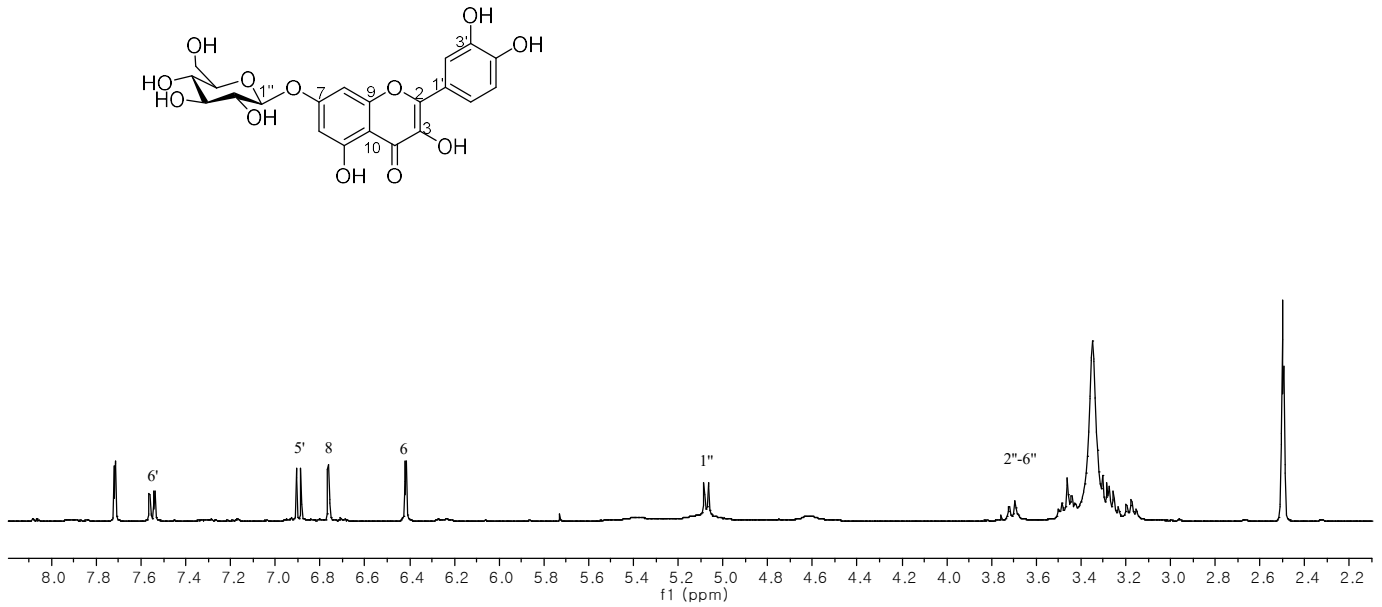


Figure 41. ^{1}H NMR spectrum of compound **19** (300 MHz, DMSO-d_6)

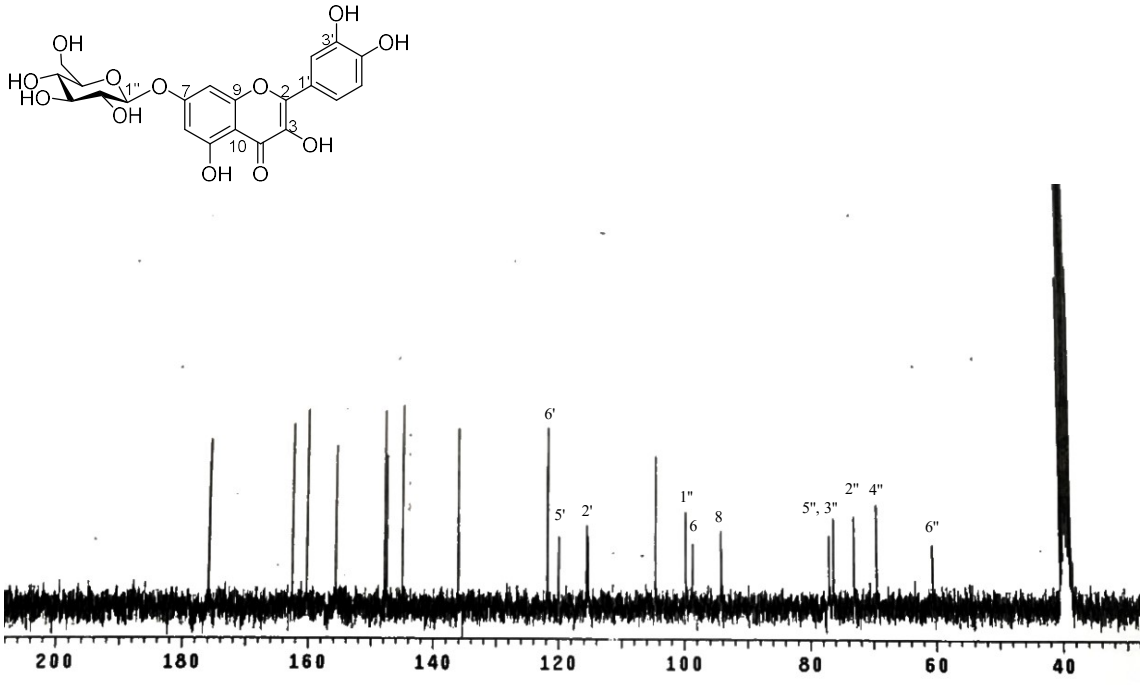


Figure 42. ^{13}C NMR spectrum of compound **19** (75 MHz, DMSO-d_6)

3.16. Compound 20

Compound **20** was obtained as yellow amorphous powder with molecular formula $C_{21}H_{20}O_{11}$, based on the *m/z* 447.1 $[M-H]^-$ in ESIMS. Based on ^1H NMR spectrum, flavonol moiety was established [two meta-coupled aromatic protons at δ_H 6.80 (1H, d, *J* = 2.1Hz, H-8) and 6.42 (1H, *J* = 2.1Hz, H-6), 1,4-disubstituted benzene ring at δ_H 8.07 (2H, d, *J* = 8.9 Hz, H-2' and H-6'), δ_H 6.94 (2H, d, *J* = 8.9 Hz, H-3' and H-5')]. The ^1H NMR spectrum also showed an anomeric proton signal at δ_H 5.06 (1H, d, *J* = 7.2Hz, H-1''). The ^{13}C NMR spectrum showed glucosyl moiety [δ_C 99.8 (C-1''), δ_C 73.1 (C-2''), δ_C 76.4 (C-3''), δ_C 69.6 (C-4''), δ_C 77.1 (C-5''), δ_C 60.6 (C-6'')]. With ^1H and ^{13}C NMR spectra, the structure of compound **20** was assigned as kaempferol-7-*O*-*β*-D-glucopyranoside. (Pereira et al. 2012)

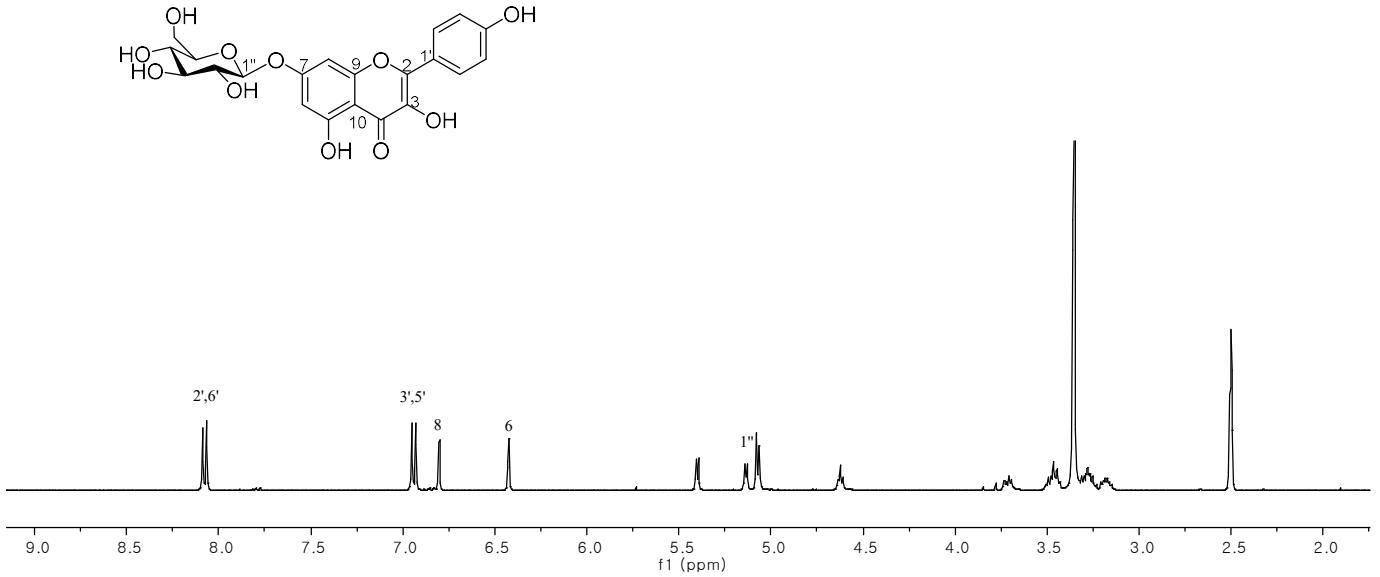


Figure 43. ^{1}H NMR spectrum of compound **20** (300 MHz, DMSO-d_6)

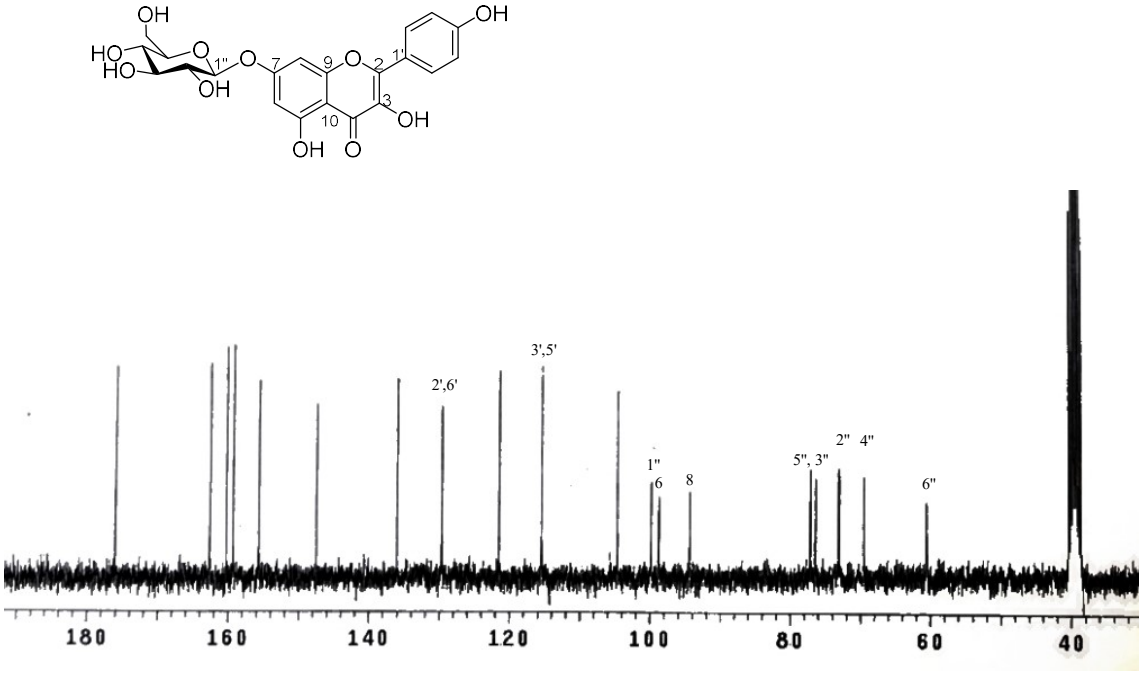


Figure 44. ^{13}C NMR spectrum of compound **20** (75 MHz, DMSO-d_6)

3.17. Compound 21

Compound **21** was obtained as yellow amorphous powder with molecular formula $C_{27}H_{30}O_{15}$, based on the *m/z* 617.2 $[M+Na]^+$ in ESIMS. Based on ^1H NMR spectrum, flavonol moiety was established [two meta-coupled aromatic protons at δ_H 6.41 (1H, d, *J* = 2.1Hz, H-8) and 6.20 (1H, *J* = 2.1Hz, H-6), 1,4-disubstituted benzene ring at δ_H 7.98 (2H, d, *J* = 8.9 Hz, H-2' and H-6'), δ_H 6.89 (2H, d, *J* = 8.9 Hz, H-3′ and H-5')]. The ^1H NMR spectrum also showed two anomeric proton signals at δ_H 5.31 (1H, d, *J* = 7.4Hz, H-1'') and δ_H 4.38 (1H, d, *J* = 1.2Hz, H-1'''). Based on ^{13}C NMR, One is glucosyl moiety [δ_C 74.2 (C-2''), δ_C 76.4 (C-3''), δ_C 70.3 (C-4''), δ_C 76.1 (C-5''), δ_C 66.9 (C-6'')], another is rhamnosyl moiety[δ_C 70.3 (C-2'''), δ_C 70.7 (C-3'''), δ_C 72.1 (C-4'''), δ_C 68.3 (C-5'''), δ_C 17.8 (C-6''')].With ^1H and ^{13}C NMR spectra, the structure of compound **21** was assigned as nicotiflorin. (Chemam et al. 2017)

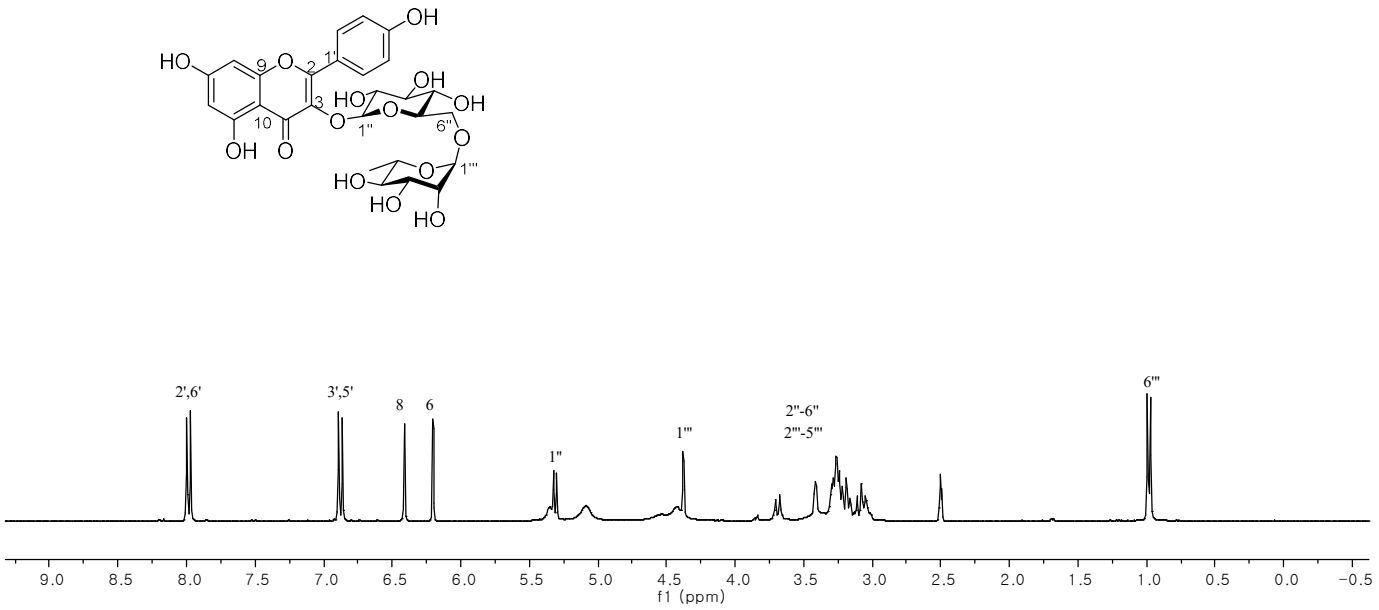


Figure 45. ^{1}H NMR spectrum of compound **21** (300 MHz, DMSO-d_6)

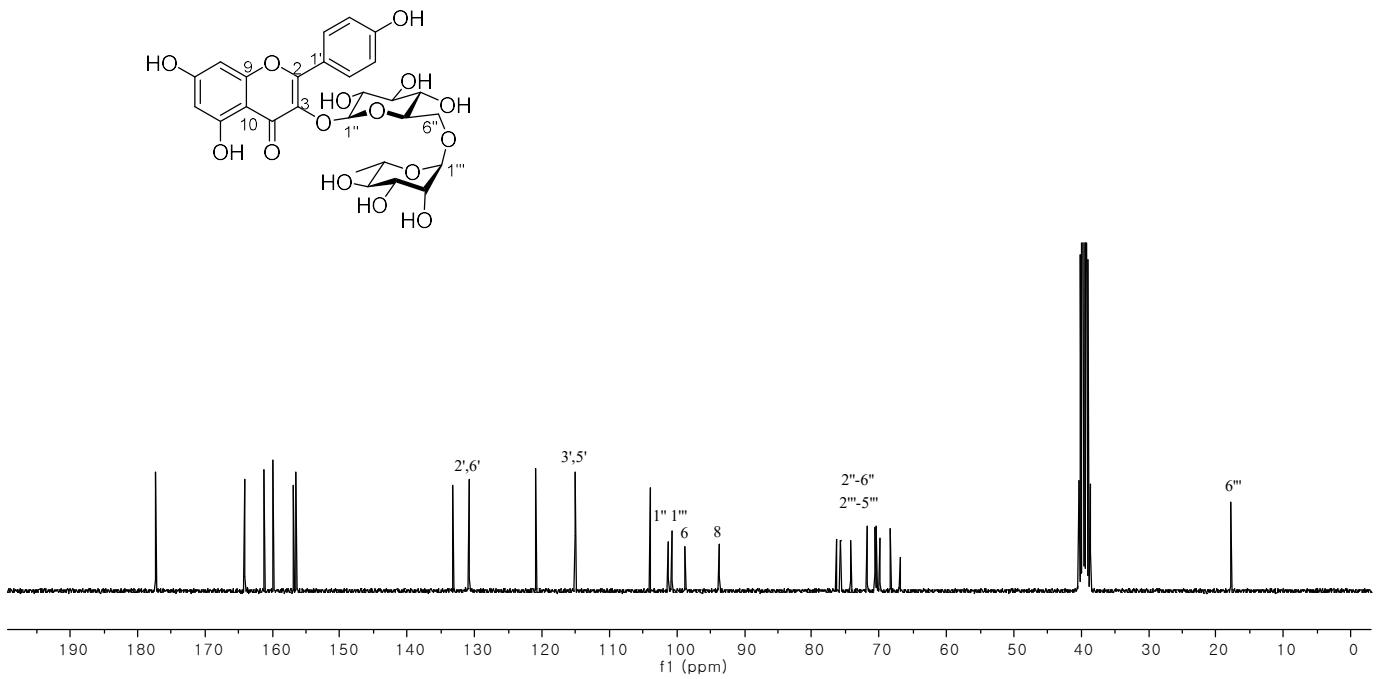


Figure 46. ^{13}C NMR spectrum of compound **21** (75 MHz, DMSO-d_6)

3.18. Compounds 22-24

Compound **22** was obtained as yellow amorphous powder with molecular formula $C_{15}H_{12}O_6$, based on the *m/z* 287.1 $[M-H]^-$ in ESIMS.. Based on ^1H NMR spectrum, flavonol moiety was established [two meta-coupled aromatic protons at δ_H 5.92 (1H, d, *J* = 2.2Hz, H-8) and 5.87 (1H, *J* = 2.2Hz, H-6), 1,4-disubstituted benzene ring at δ_H 7.32 (2H, d, *J* = 8.5 Hz, H-2' and H-6'), δ_H 6.79 (2H, d, *J* = 8.5 Hz, H-3' and H-5'), two methane protons at δ_H 5.05 (1H, d, *J* = 11.4Hz, H-2) and δ_H 4.58 (1H, d, *J* = 11.4Hz, H-3)]. With ^1H and ^{13}C NMR spectra, the structure of compound **22** was assigned as aromadendrin. (Yoon et al. 2007)

Compound **23** was obtained as yellow amorphous powder with molecular formula $C_{21}H_{22}O_{11}$, based on the *m/z* 449.1 $[M-H]^-$ in ESIMS. The ^1H NMR spectrum of **23** was similar to that of **22**, except an anomeric proton signal at δ_H 4.97 (1H, d, *J* = 7.3Hz, H-1") and glucosyl moiety [δ_C 99.6 (C-1"), δ_C 73.0 (C-2"), δ_C 76.4 (C-3"), δ_C 69.5 (C-4"), δ_C 77.1 (C-5"), δ_C 60.6 (C-6")]. With ^1H and ^{13}C NMR spectra, the structure of compound **23** was assigned as aromadendrin-7-*O*-*β*-D-glucopyranoside. (Huang et al. 2013)

Compound **24** was obtained as white amorphous powder with molecular formula $C_{22}H_{18}O_7$, based on the *m/z* 393.1 $[M-H]^-$ in ESIMS. The ^1H NMR spectrum of **24** was similar to that of **22**, except *p*-hydroxybenzyl substituent on C-6 (δ_C 111.3) [1,4-disubstituted benzene ring at δ_H 7.09 (2H, d, *J* = 8.5 Hz, H-3" and H-7") and δ_H 6.61 (2H, d, *J* = 8.5 Hz, H-4" and H-6") and methylene protons at δ_H 7.57 (2H, m, H-1")]. With ^1H and ^{13}C NMR spectra, the structure of compound **24** was assigned as gericudranin E. (Lee et al. 1995)

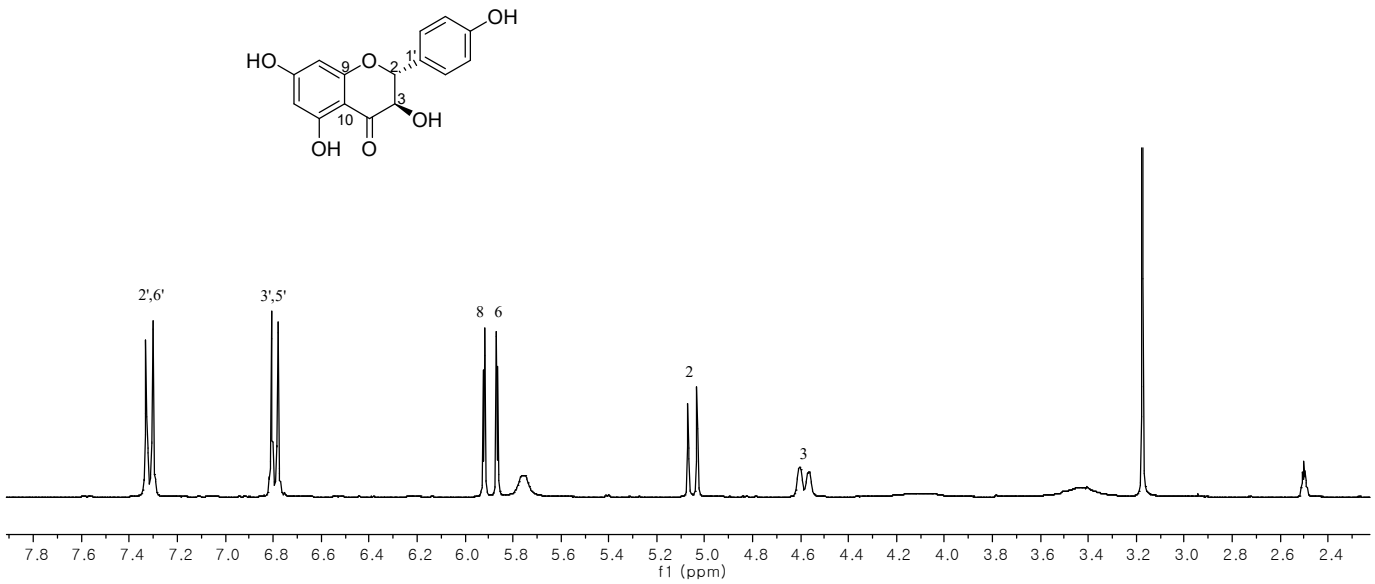


Figure 47. ^{1}H NMR spectrum of compound **22** (300 MHz, DMSO-d_6)

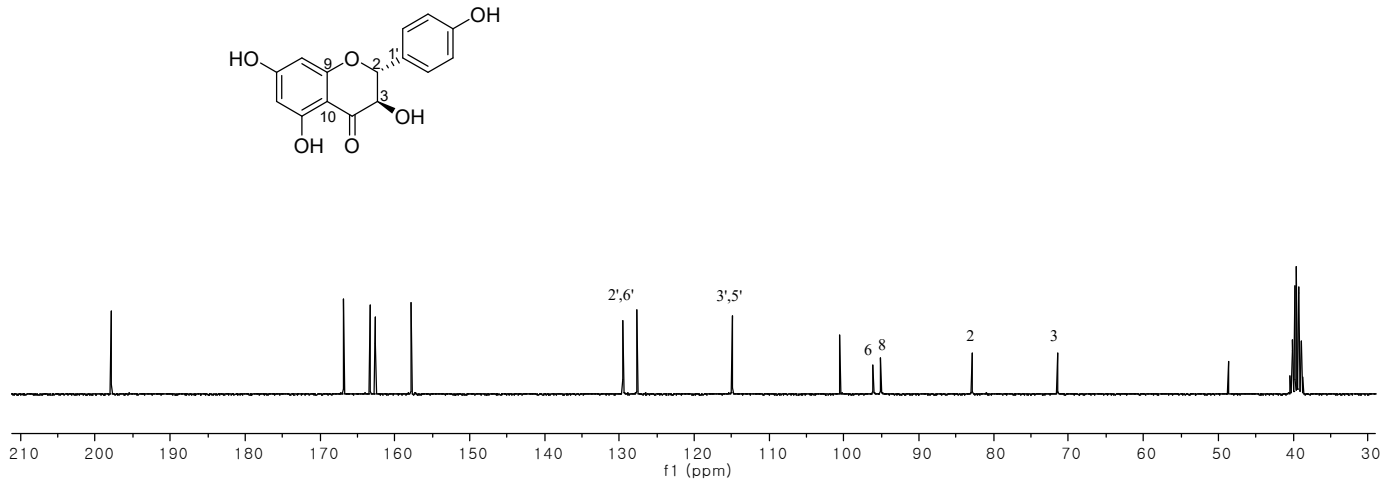


Figure 48. ^{13}C NMR spectrum of compound **22** (75 MHz, DMSO-d_6)

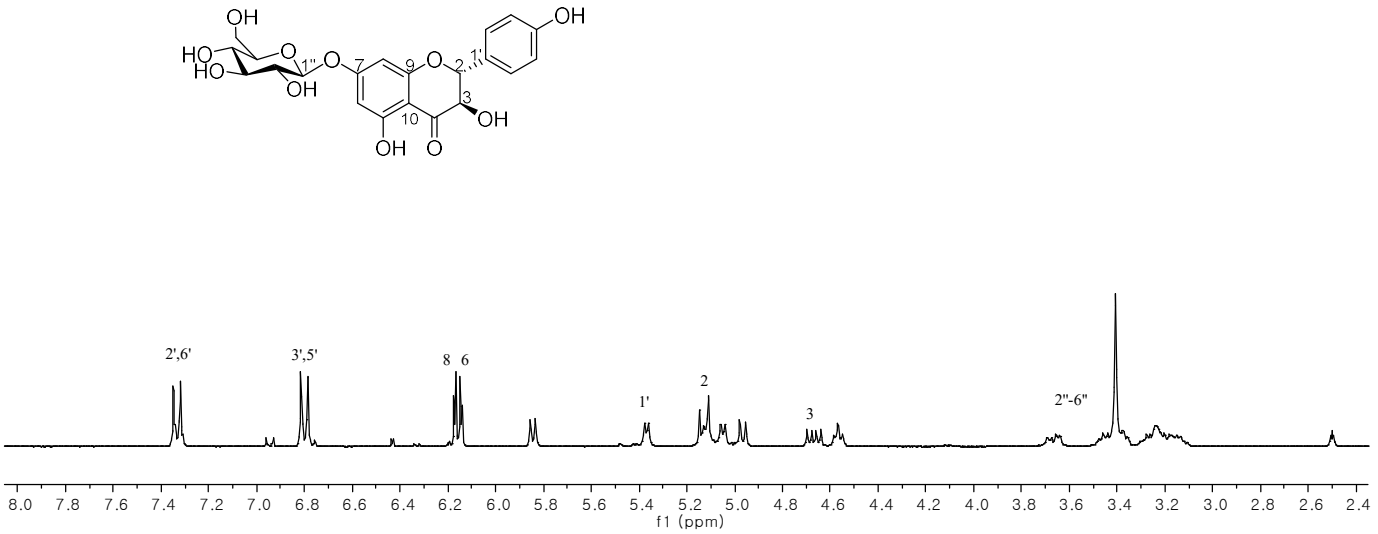


Figure 49. ^{1}H NMR spectrum of compound **23** (300 MHz, DMSO-d_6)

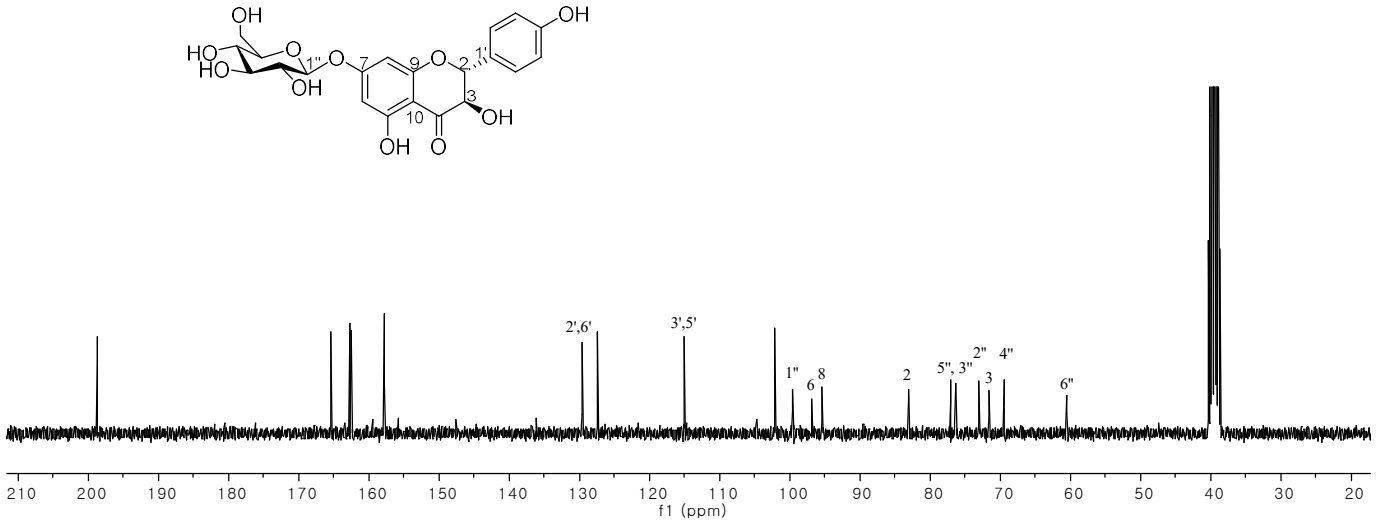


Figure 50. ^{13}C NMR spectrum of compound **23** (75 MHz, DMSO-d_6)

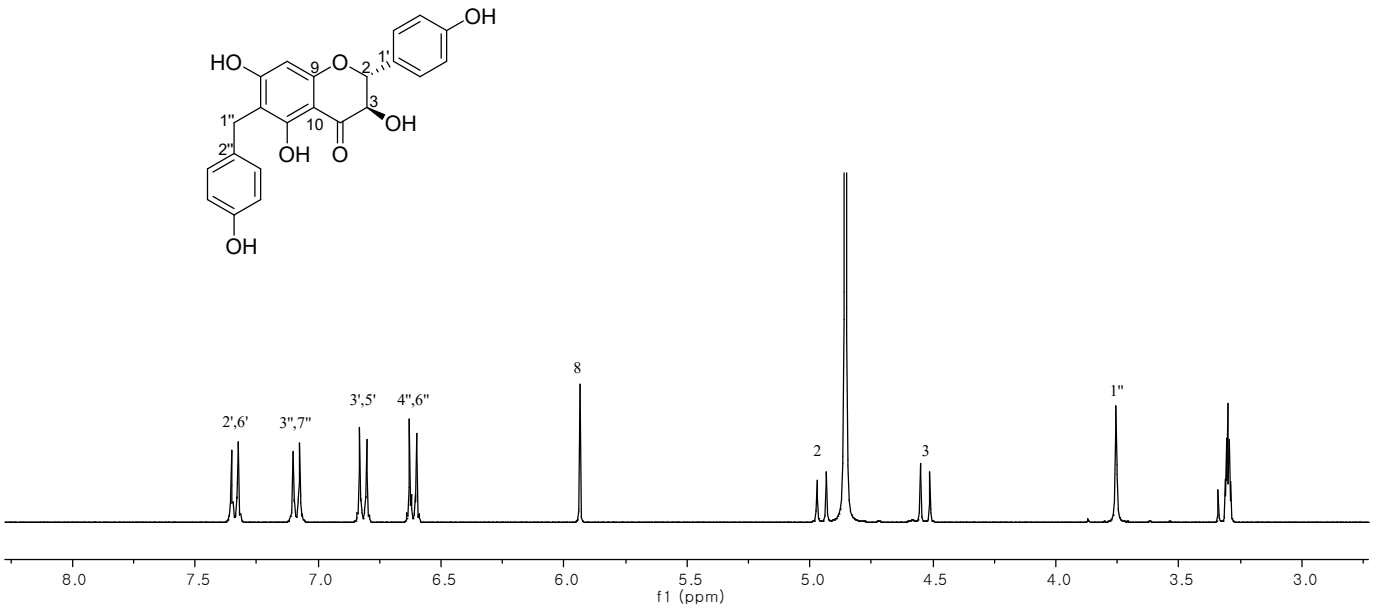


Figure 51. ^{1}H NMR spectrum of compound **24** (300 MHz, CD_3OD)

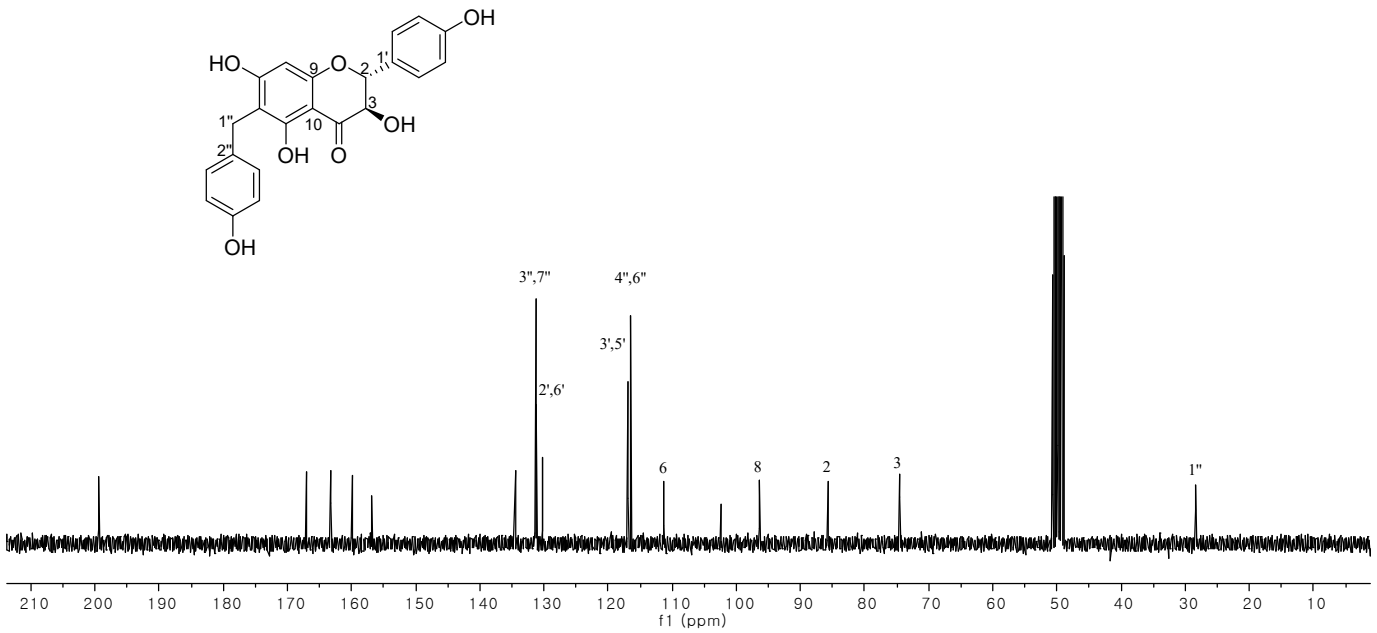


Figure 52. ^{13}C NMR spectrum of compound **24** (75 MHz, CD_3OD)

3.19. Compound 25

Compound **25** was obtained as dark yellow amorphous powder with molecular formula $C_{15}H_{12}O_7$, based on the *m/z* 303.1 $[M-H]^-$ in ESIMS. Based on ^1H NMR spectrum, flavanol moiety was established [two meta-coupled aromatic protons at δ_H 5.92 (1H, d, *J* = 1.9Hz, H-8) and δ_H 5.88 (1H, d, *J* = 1.9Hz, H-6), 1,3,4-trisubstituted benzene ring at δ_H 6.96 (1H, d, *J* = 1.5 Hz, H-2'), δ_H 6.85 (1H, d, *J* = 8.1Hz, H-6') and δ_H 6.80 (1H, dd, *J* = 8.1Hz, 1.5 Hz, H-5') , two methane protons at δ_H 4.91 (1H, d, *J* = 11.5Hz, H-2) and δ_H 4.50 (1H, d, *J* = 11.5Hz, H-3)]. With ^1H and ^{13}C NMR spectra, the structure of compound **25** was assigned as taxifolin. (Hendra et al. 2017)

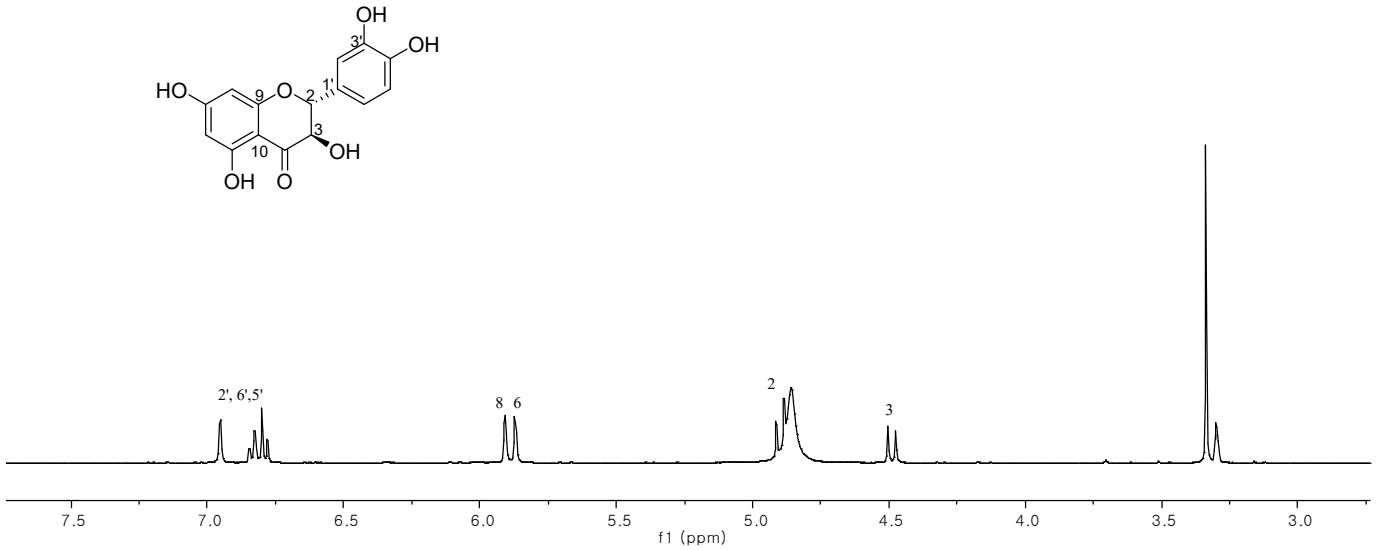


Figure 53. ^{1}H NMR spectrum of compound **25** (300 MHz, CD_3OD)

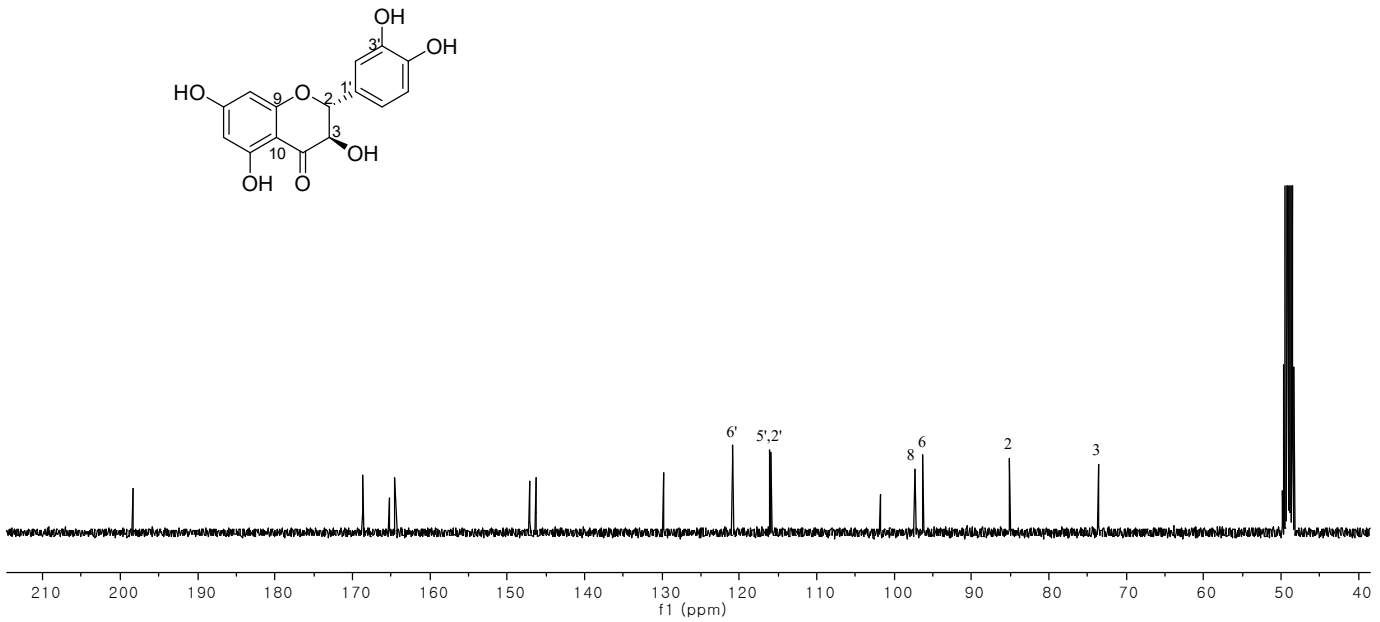


Figure 54. ^{13}C NMR spectrum of compound **25** (75 MHz, CD_3OD)

3.20. Compound 26

Compound **26** was obtained as dark yellow amorphous powder with molecular formula $C_{15}H_{12}O_7$, based on the *m/z* 303.1 $[M-H]^-$ in ESIMS. Based on ^1H NMR spectrum, flavanol moiety was established [two meta-coupled aromatic protons at δ_H 5.91 (1H, d, *J* = 2.1Hz, H-8) and δ_H 5.87 (1H, d, *J* = 2.1Hz, H-6), 1,3,4-trisubstituted benzene ring at δ_H 7.22 (1H, d, *J* = 9.0 Hz, H-6'), δ_H 6.34 (1H, m, H-3') and δ_H 6.34 (1H, m, H-5'), two methane protons at δ_H 5.39 (1H, d, *J* = 11.4Hz, H-2) and δ_H 4.79 (1H, d, *J* = 11.4Hz, H-3)]. With ^1H and ^{13}C NMR spectra, the structure of compound **26** was assigned as dihydromorin. (Zheng et al. 2008)

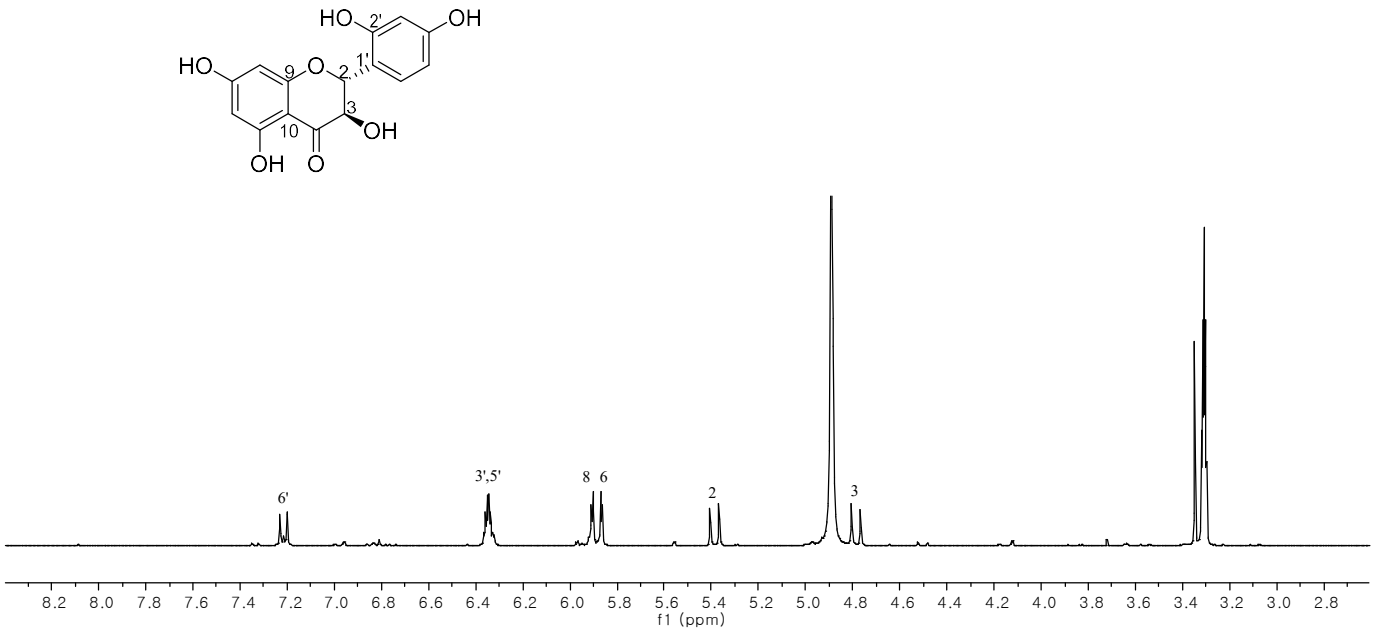


Figure 55. ^{1}H NMR spectrum of compound **26** (300 MHz, CD_3OD)

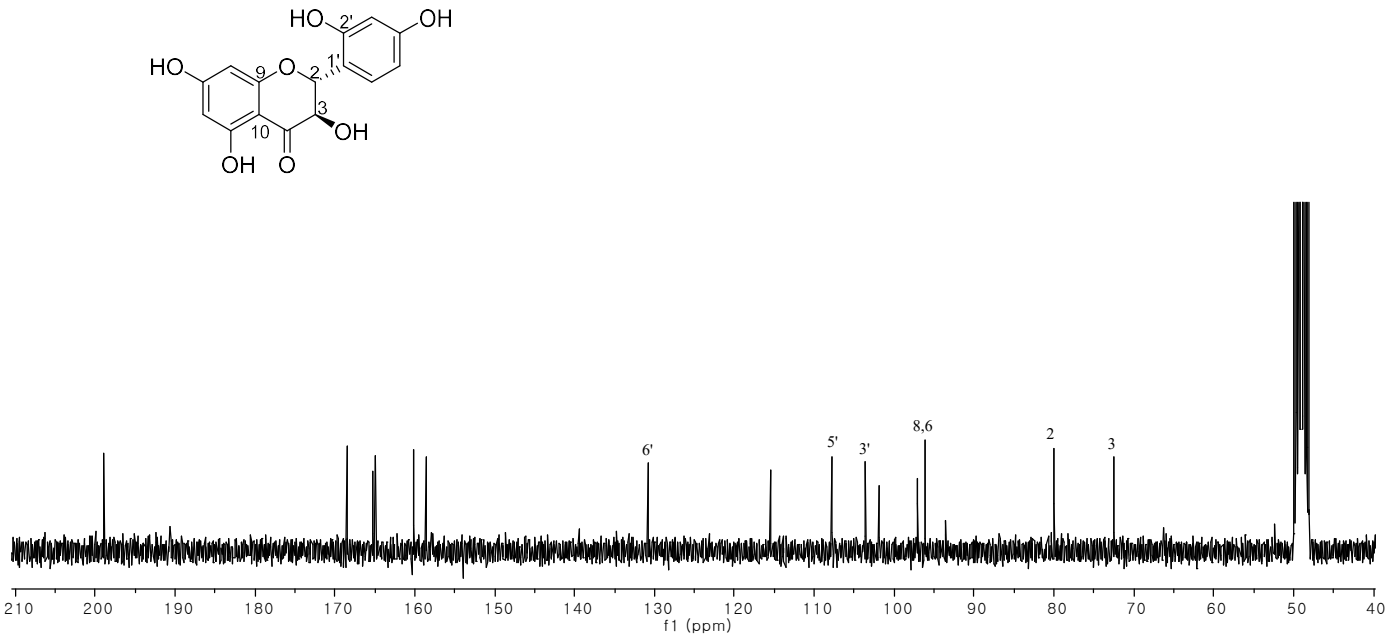


Figure 56. ^{13}C NMR spectrum of compound **26** (75 MHz, CD_3OD)

3.21. Compound 27-28

Compound **27** was obtained as dark yellow amorphous powder with molecular formula $C_{15}H_{10}O_6$, based on the *m/z* 285.0 $[M-H]^-$ in ESIMS. Based on ^1H NMR spectrum, isoflavone moiety was established [two meta-coupled aromatic protons at δ_H 6.33 (1H, d, *J* = 1.9 Hz, H-8) and δ_H 6.21 (1H, d, *J* = 1.9 Hz, H-6), 1,3,4-trisubstituted benzene ring at δ_H 7.02 (1H, m, H-2'), δ_H 6.83 (1H, m, H-5') and δ_H 6.83 (1H, m, H-6'), Olefinic proton at δ_H 8.03 (1H, s, H-2)]. With ^1H and ^{13}C NMR spectra, the structure of compound **27** was assigned as orobol. (Lima et al. 2016)

Compound **28** was obtained as dark yellow amorphous powder with molecular formula $C_{21}H_{20}O_{11}$, based on the *m/z* 447.1 $[M-H]^-$ in ESIMS. The ^1H NMR spectrum of **28** was similar to that of **27**, except an anomeric proton signal at δ_H 5.07 (1H, d, *J* = 7.2Hz, H-1") and glucosyl moiety [δ_C 100.8 (C-1"), δ_C 73.1 (C-2"), δ_C 76.4 (C-3"), δ_C 69.6 (C-4"), δ_C 77.2 (C-5"), δ_C 60.6 (C-6")]. With ^1H and ^{13}C NMR spectra, the structure of compound **28** was assigned as orobol-7-*O*-*β*-D-glucopyranoside. (Chiang et al. 2016)

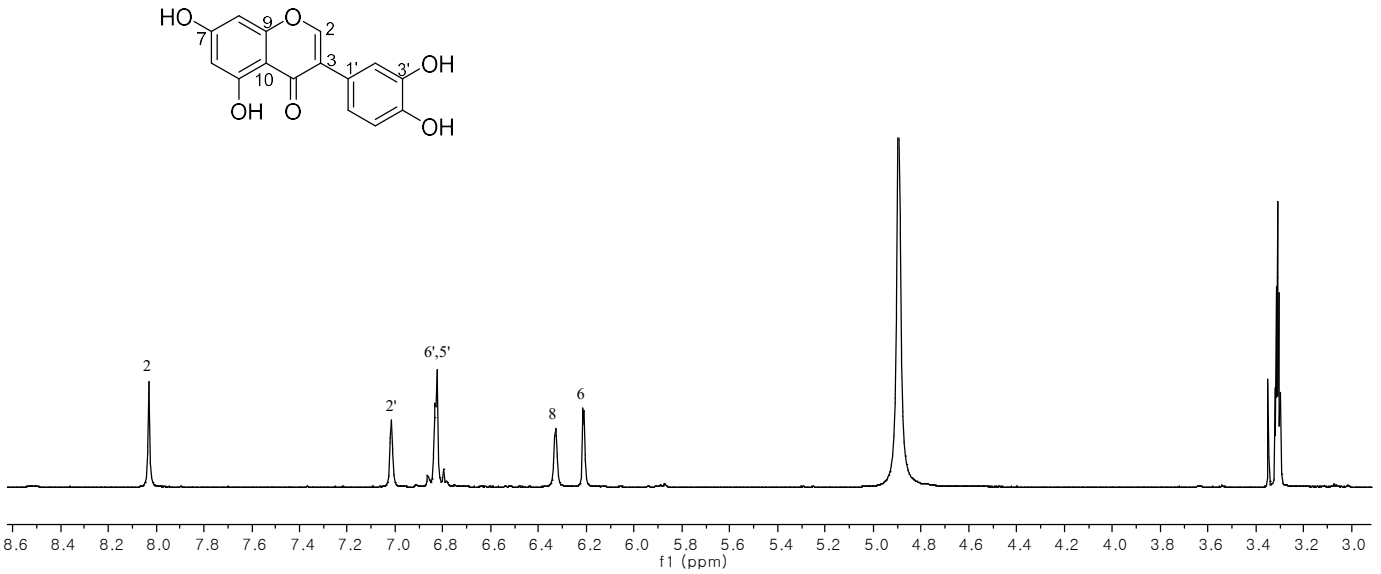


Figure 57. ^{1}H NMR spectrum of compound **27** (300 MHz, CD_3OD)

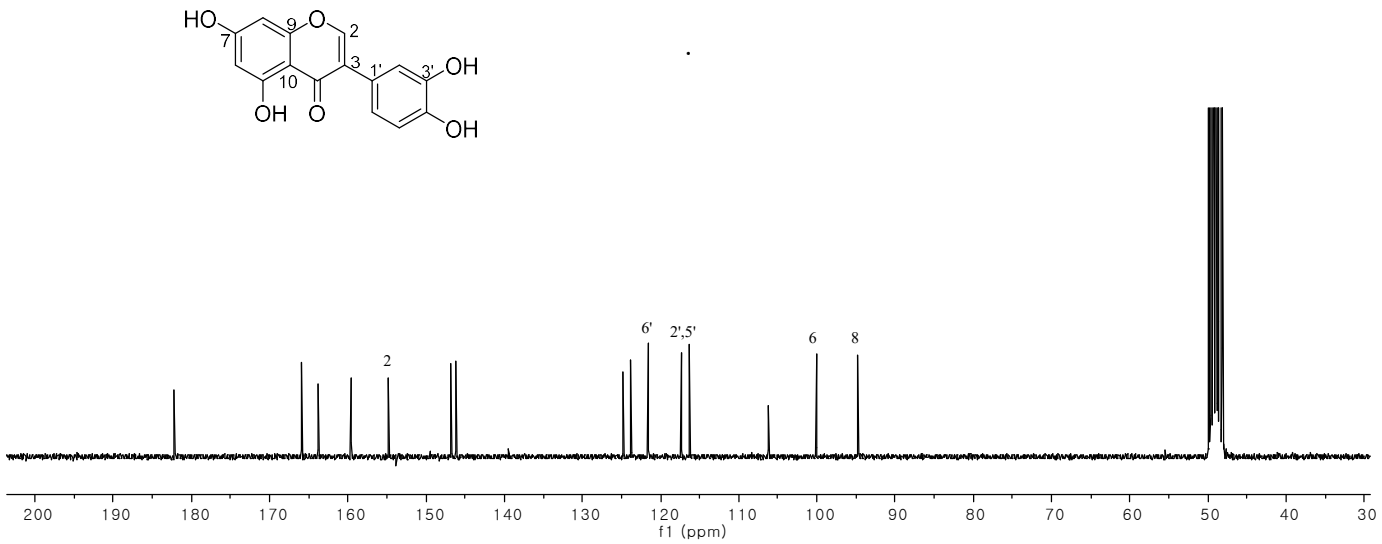


Figure 58. ^{13}C NMR spectrum of compound **27** (75 MHz, CD_3OD)

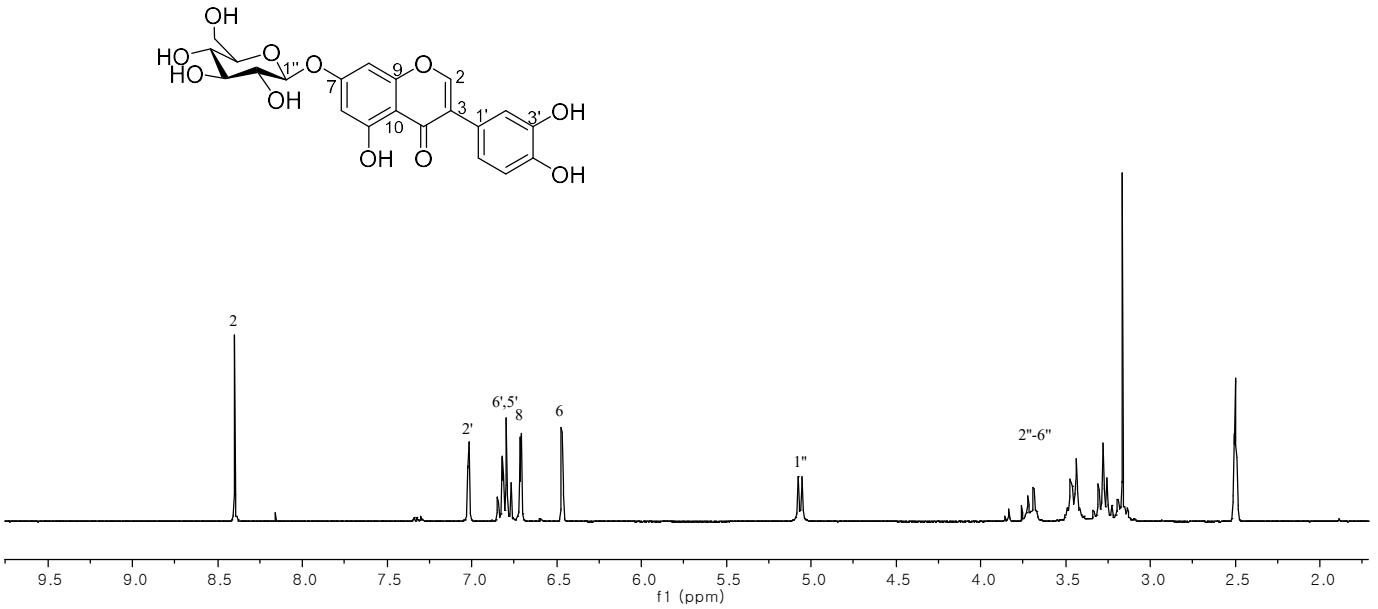


Figure 59. ^{1}H NMR spectrum of compound **28** (300 MHz, CD_3OD)

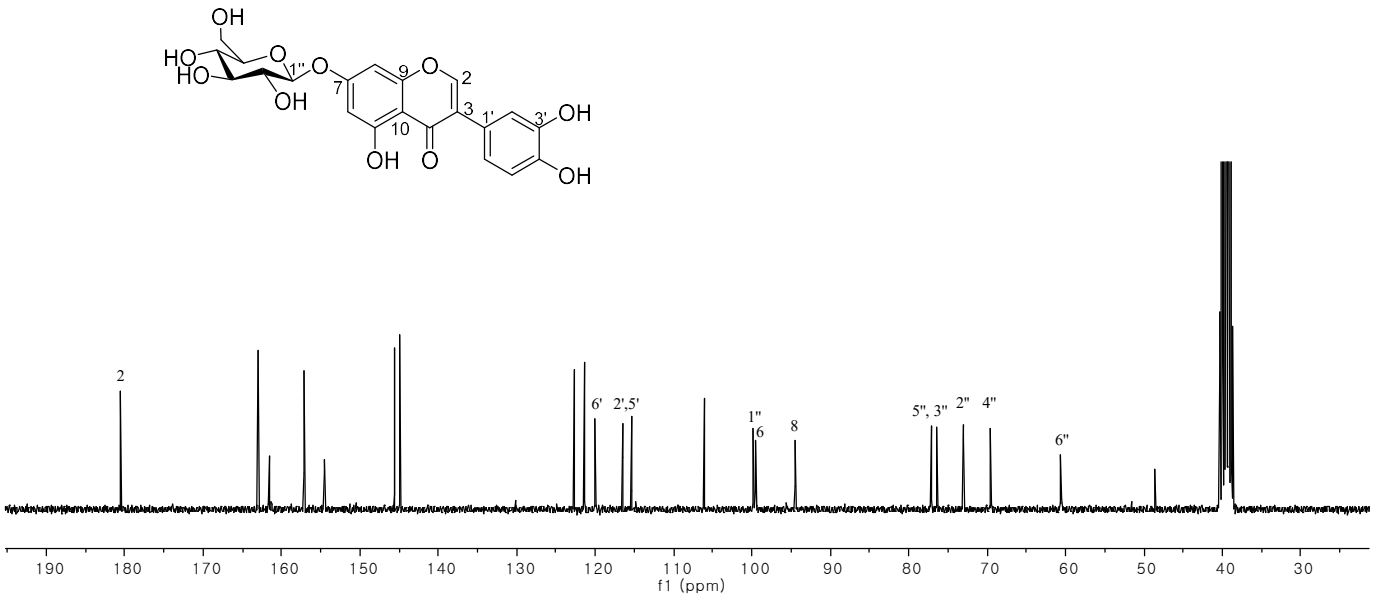


Figure 60. ^{13}C NMR spectrum of compound **28** (75 MHz, CD_3OD)

3.22. Compound 29

Compound **29** was obtained as colorless amorphous powder with molecular formula $C_{26}H_{28}O_{14}$, based on the *m/z* 563.1 $[M-H]^-$ in ESIMS.. Based on ^1H NMR spectrum, isoflavone moiety was established [two meta-coupled aromatic protons at δ_H 6.73 (1H, d, *J* = 2.0 Hz, H-8) and δ_H 6.46 (1H, d, *J* = 2.0 Hz, H-6), 1,4-disubstituted benzene ring at δ_H 7.40 (2H, *J* = 8.5Hz, H-2' and H-6'), δ_H 6.83 (2H, *J* = 8.5Hz, H-3' and H-5'), Olefinic proton at δ_H 8.13 (1H, s, H-2)]. The ^1H NMR spectrum also showed two anomeric proton signals at δ_H 5.04 (1H, d, *J* = 7.2Hz, H-1") and δ_H 4.81 (1H, d, *J* = 3.1Hz, H-1'"). Based on ^{13}C NMR, One had glucosyl moiety [δ_C 99.6 (C-1"), δ_C 73.3 (C-2"), δ_C 76.4 (C-3"), δ_C 69.9 (C-4"), δ_C 75.6 (C-5"), δ_C 67.7 (C-6")], another had apiosyl moiety [δ_C 109.4 (C-1'"), δ_C 75.9 (C-2'"), δ_C 78.7 (C-3'"), δ_C 73.0 (C-4'"), δ_C 63.2 (C-5'")]. With ^1H and ^{13}C NMR spectra, the structure of compound **29** was assigned as ambocin. (Ma et al. 1998)

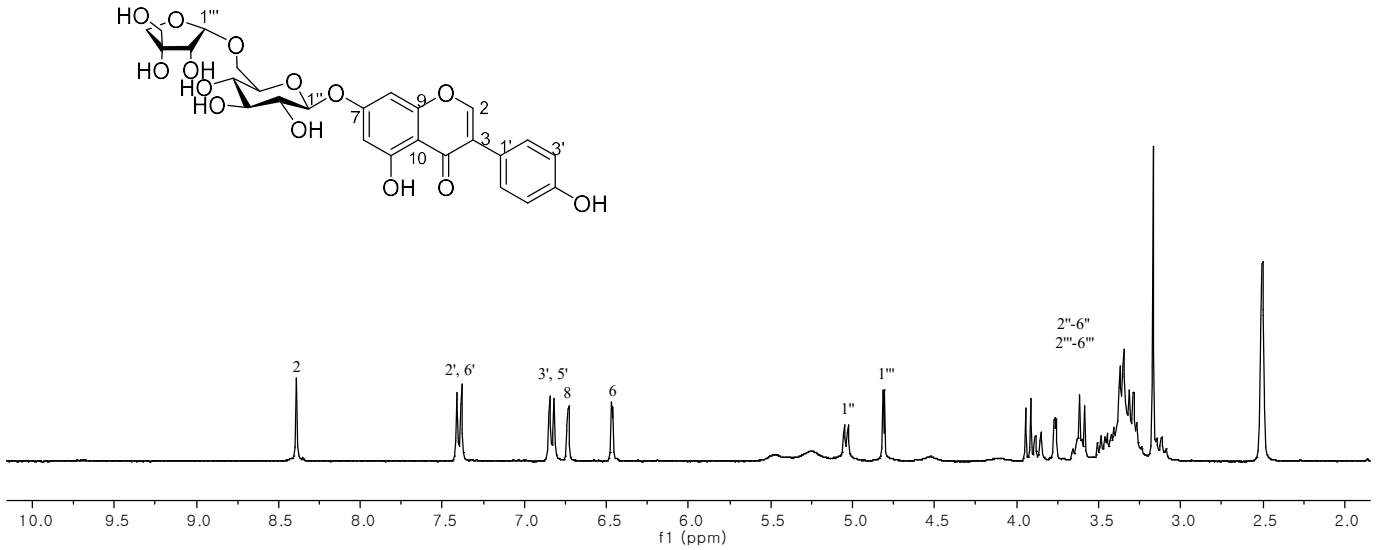


Figure 61. ^{1}H NMR spectrum of compound **29** (300 MHz, DMSO-d_6)

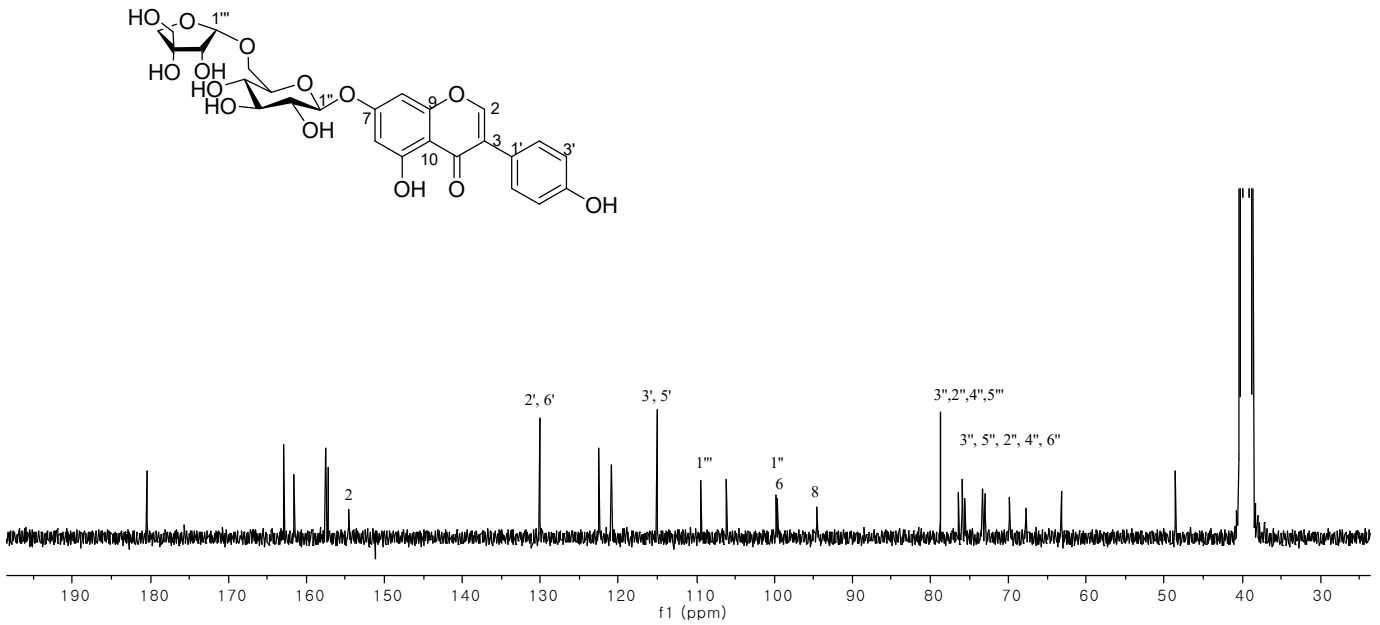


Figure 62. ^{13}C NMR spectrum of compound **29** (75 MHz, DMSO-d_6)

3.23. Compound 30

Compound **30** was obtained as yellow amorphous powder with molecular formula $C_{22}H_{28}O_{10}$, based on the *m/z* 445.1 $[M-H]^-$ in ESIMS. Based on ^1H NMR spectrum, 8-monosubstituted isoflavone moiety was established [one aromatic protons at δ_H 6.44 (1H, s, H-6) 1,4-disubstituted benzene ring at δ_H 7.31 (2H, *J* = 8.6Hz, H-2' and H-6'), δ_H 6.80 (2H, *J* = 8.6Hz, H-3' and H-5'), Olefinic proton at δ_H 7.97 (1H, s, H-2)]. The ^1H NMR spectrum also showed an anomeric proton signal at δ_H 4.99 (1H, d, *J* = 9.9Hz, H-1") and one methoxy group at δ_H 3.84 (3H, s, 5-OCH_3). The ^{13}C NMR spectrum showed glucosyl moiety [δ_C 73.9 (C-1"), δ_C 76.5 (C-2"), δ_C 80.8 (C-3"), δ_C 72.5 (C-4"), δ_C 83.4 (C-5"), δ_C 63.5 (C-6")]. With ^1H and ^{13}C NMR spectra, the structure of compound **30** was assigned as 5-methoxy-8-glucopyranosyl-genistein. (Mekkiou et al. 2005)

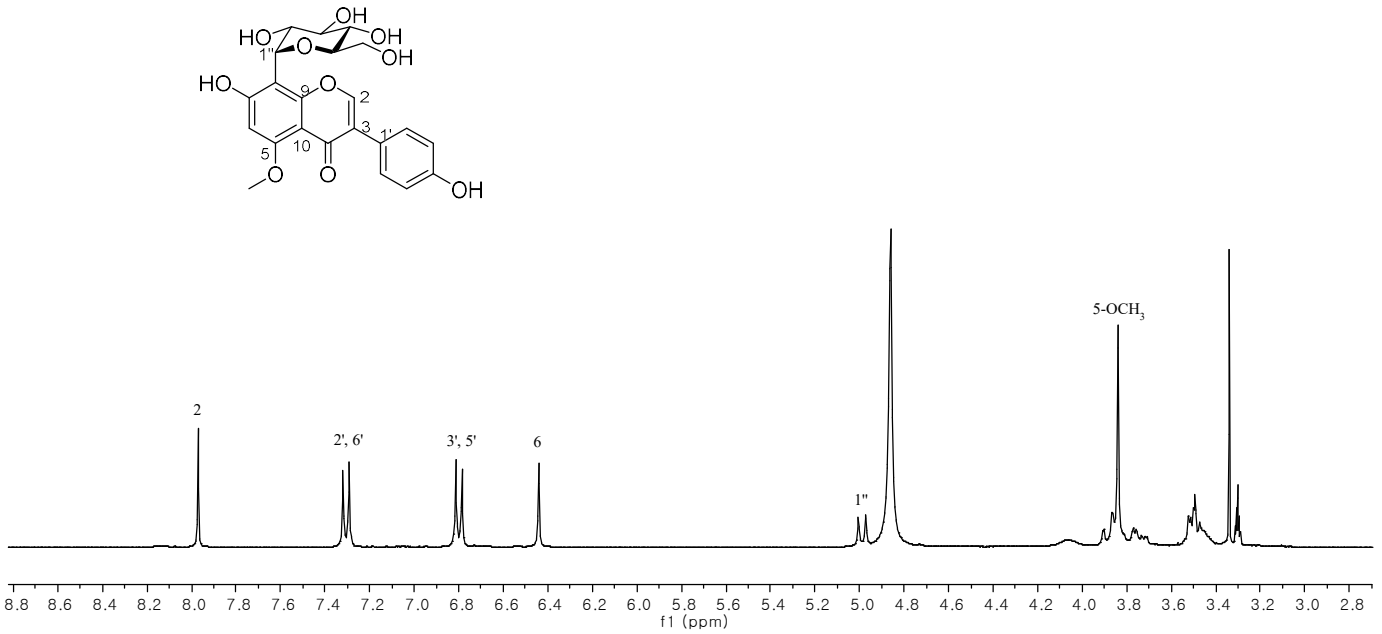


Figure 63. ^{1}H NMR spectrum of compound **30** (300 MHz, CD_3OD)

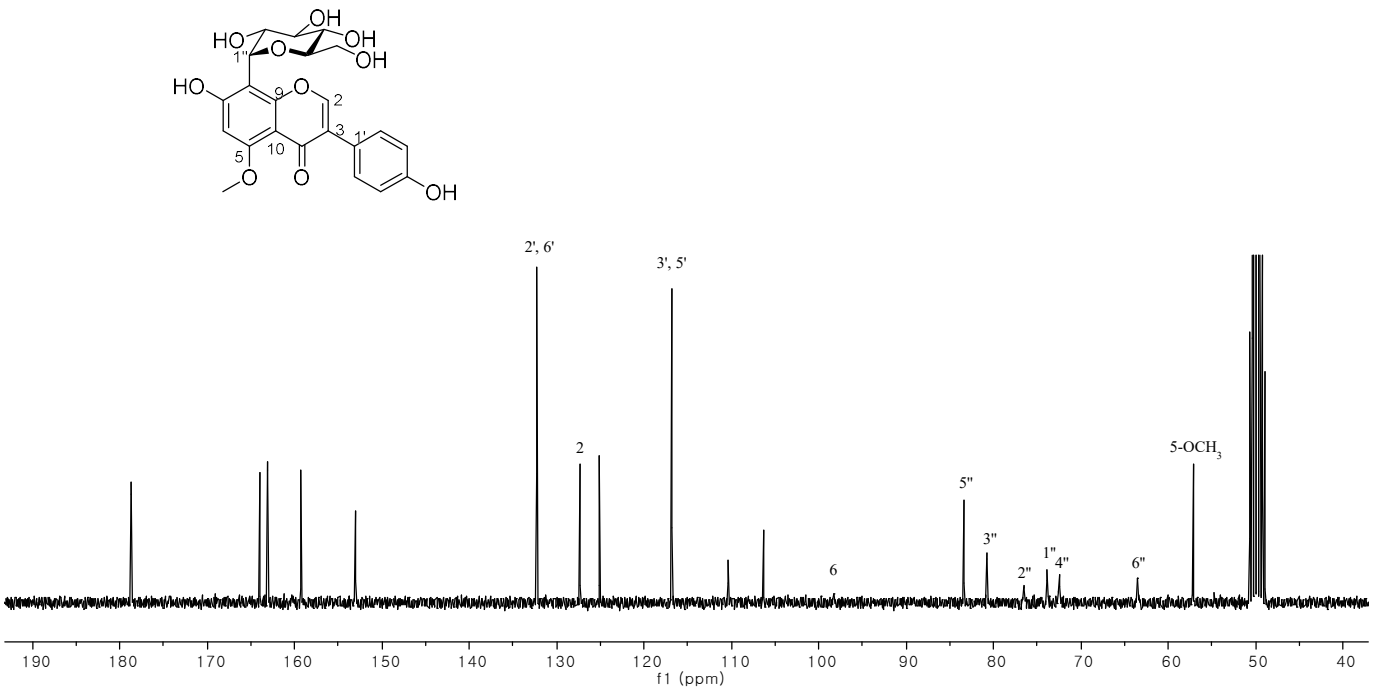


Figure 64. ^{13}C NMR spectrum of compound **30** (75 MHz, CD_3OD)

Chapter4. Conclusion

30 compounds were isolated from the EtOAC and *n*-butanol fractions of *Cudrania tricuspidata* using various chromatographic techniques. Compounds **1-5** are phenolic type, compound **6** is stilbenoid type, compound **7** is megastigmane derivative, compounds **8-9** are caffeoyl derivatives**,** compounds **10-12** are coumarin type, compounds **13-14** are phenylpropanoid type, compounds **15-16** are benzoic acid derivatives, compounds **17-30** are flavonoid type.

Compounds **1** and **2** are newly reported in nature.

Compounds **3**, **4**, **5**, **13**, **14**, **15**, **16**, **19**, **29** are newly reported from Moraceae family.

Compounds **7**, **11**, **12** are newly reported from *Cudrania* genus

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Supplementary Information

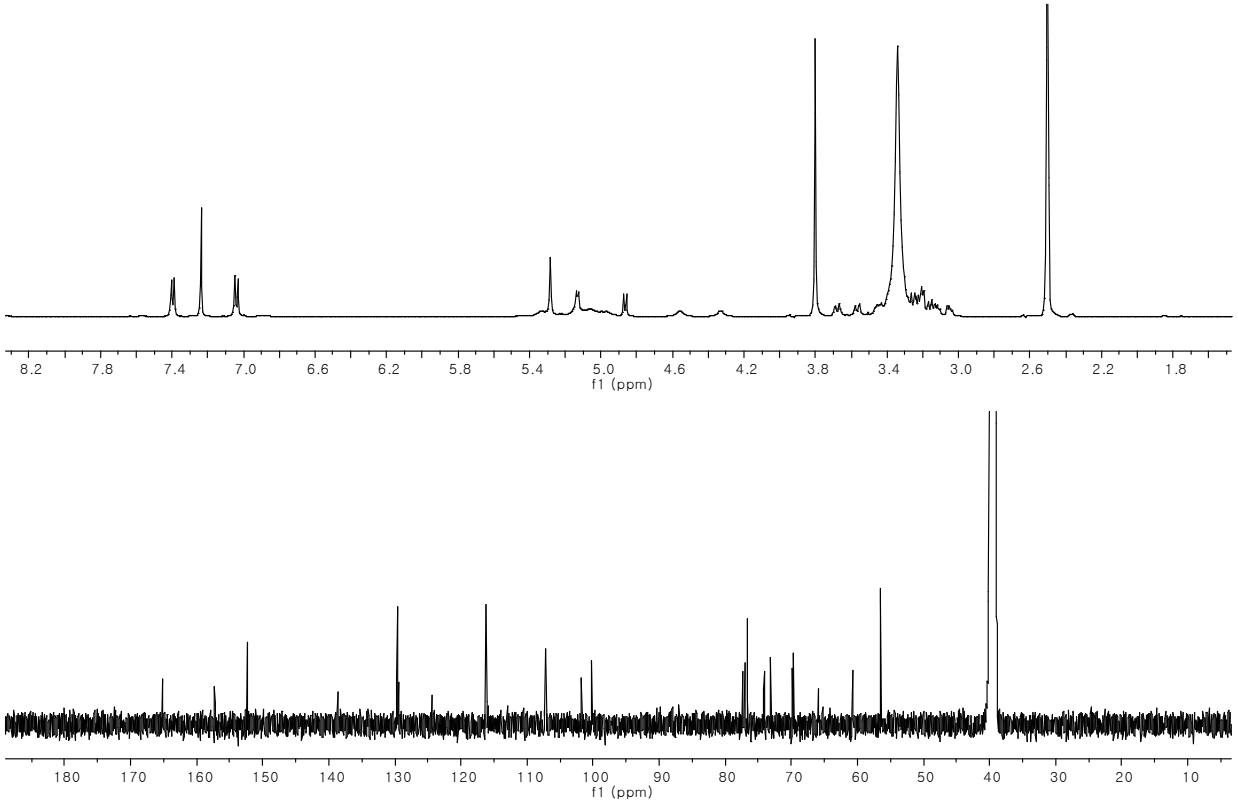

Figure 65. ^{1}H and ^{13}C NMR spectra of compound **1** (500/125 MHz, DMSO-d_6)

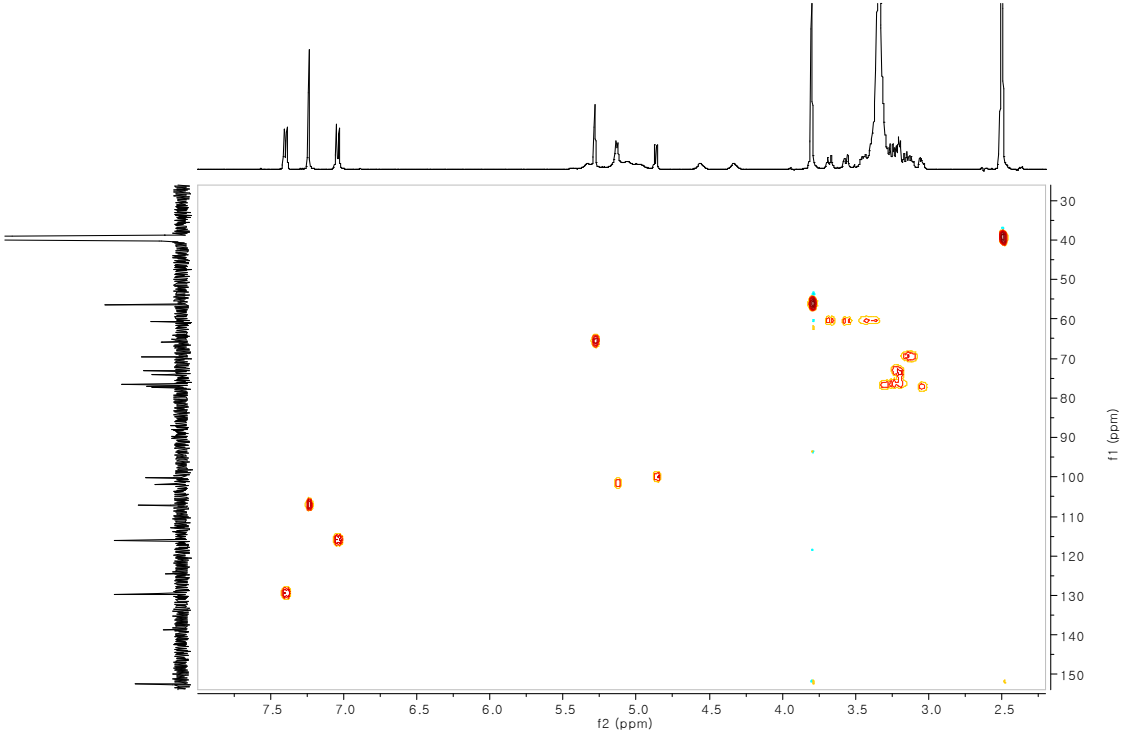

Figure 66. HSQC spectrum of compound **1** (400 MHz, DMSO-d_6)

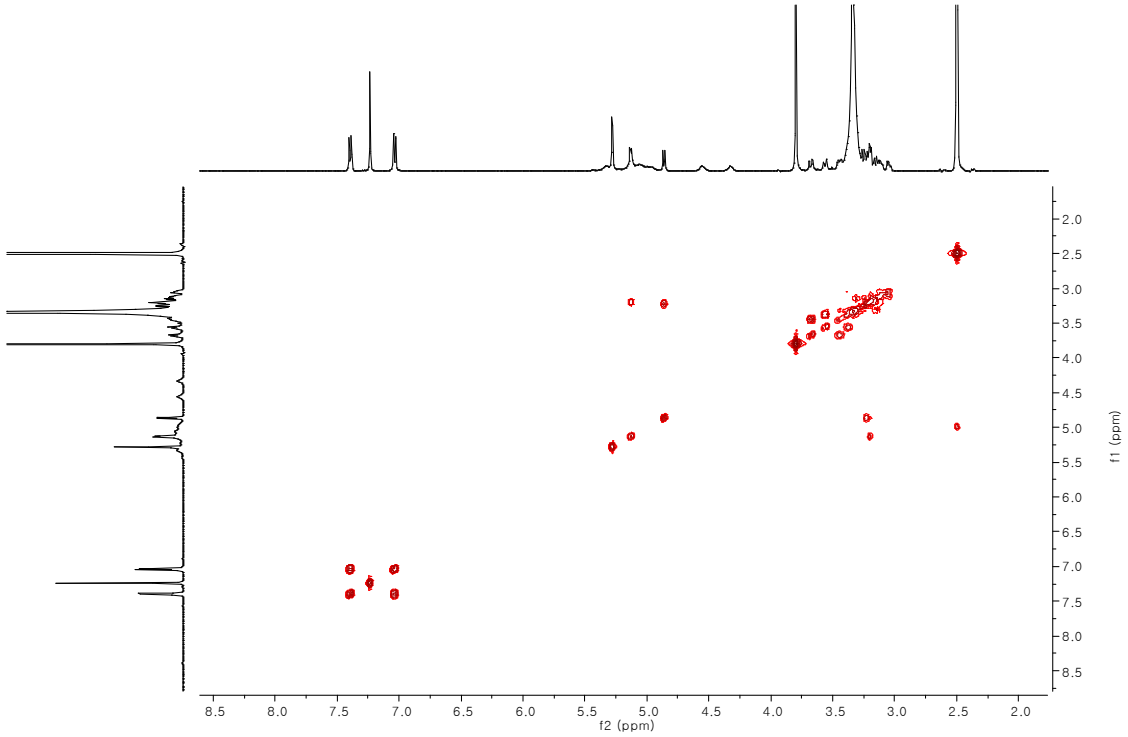

Figure 67. COSY spectrum of compound **1** (400 MHz, DMSO-d_6)

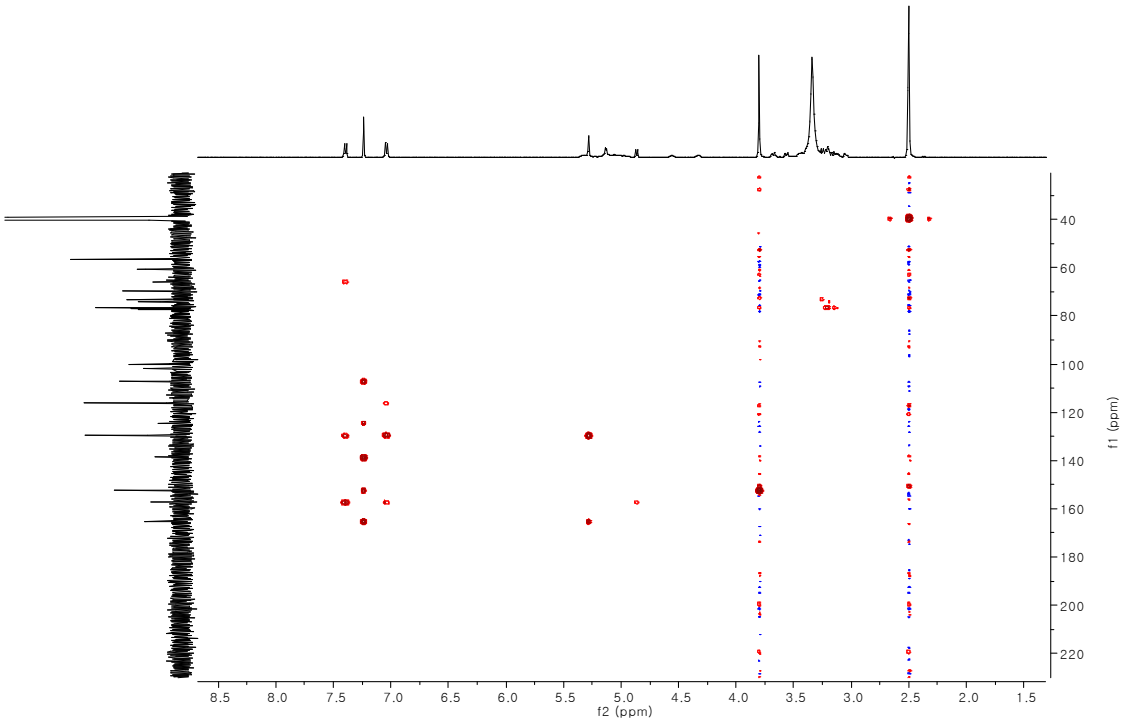

Figure 68. HMBC spectrum of compound **1** (400 MHz, DMSO-d_6)

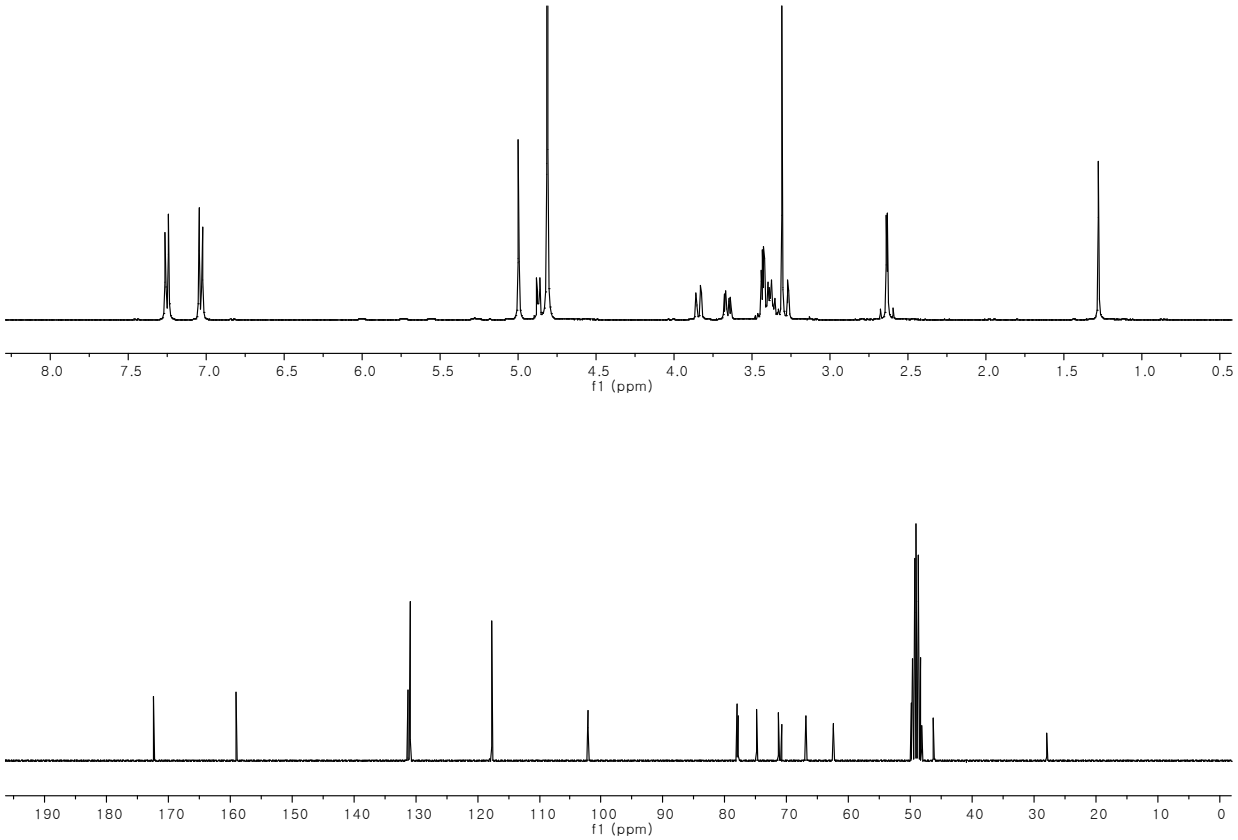

Figure 69. . ^{1}H and ^{13}C NMR spectra of compound **2** (300/75 MHz, CD_3OD)

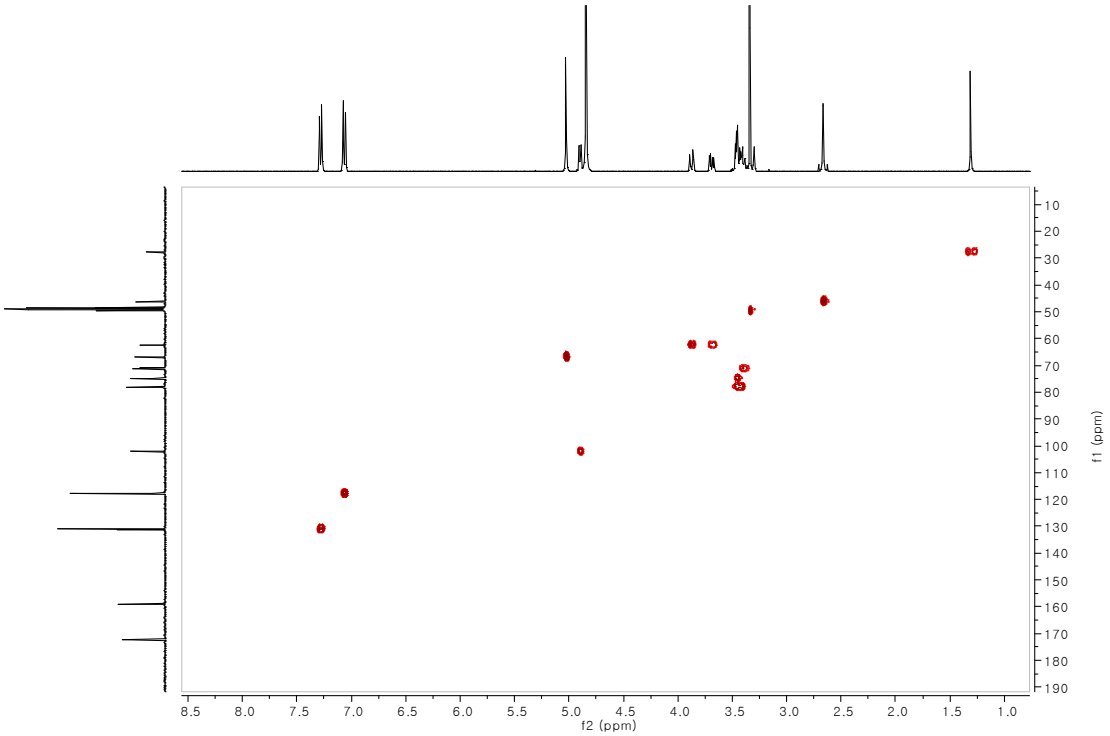

Figure 70. HSQC spectrum of compound **2** (400 MHz, CD_3OD)

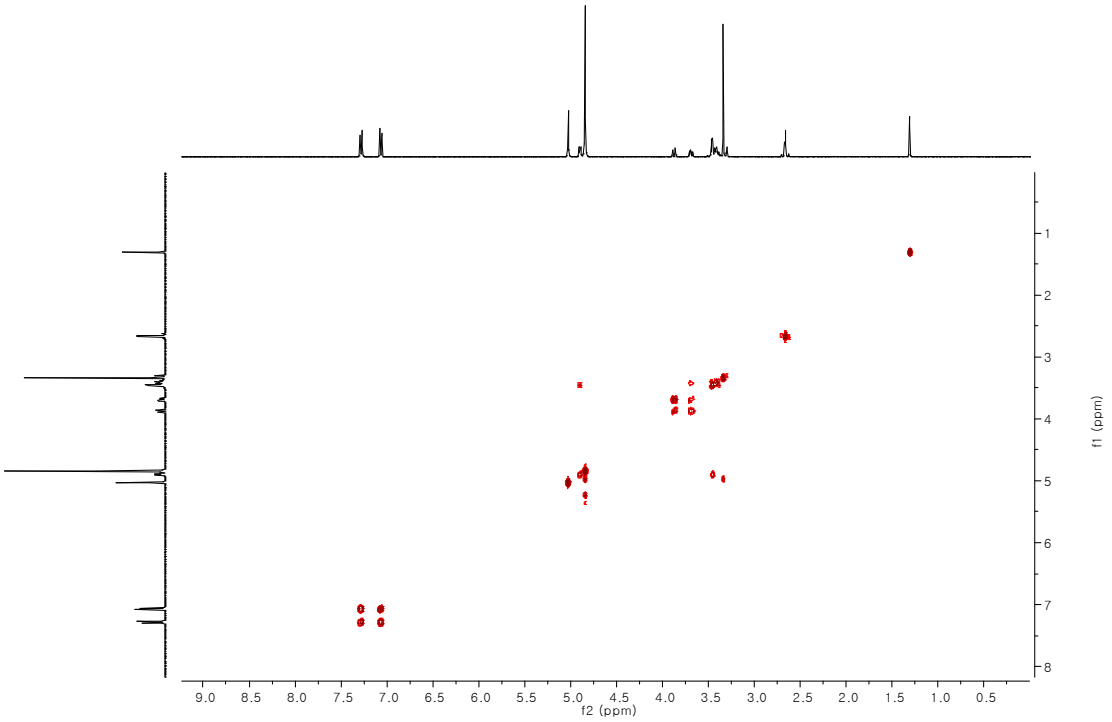

Figure 71. COSY spectrum of compound **2** (400 MHz, CD_3OD)

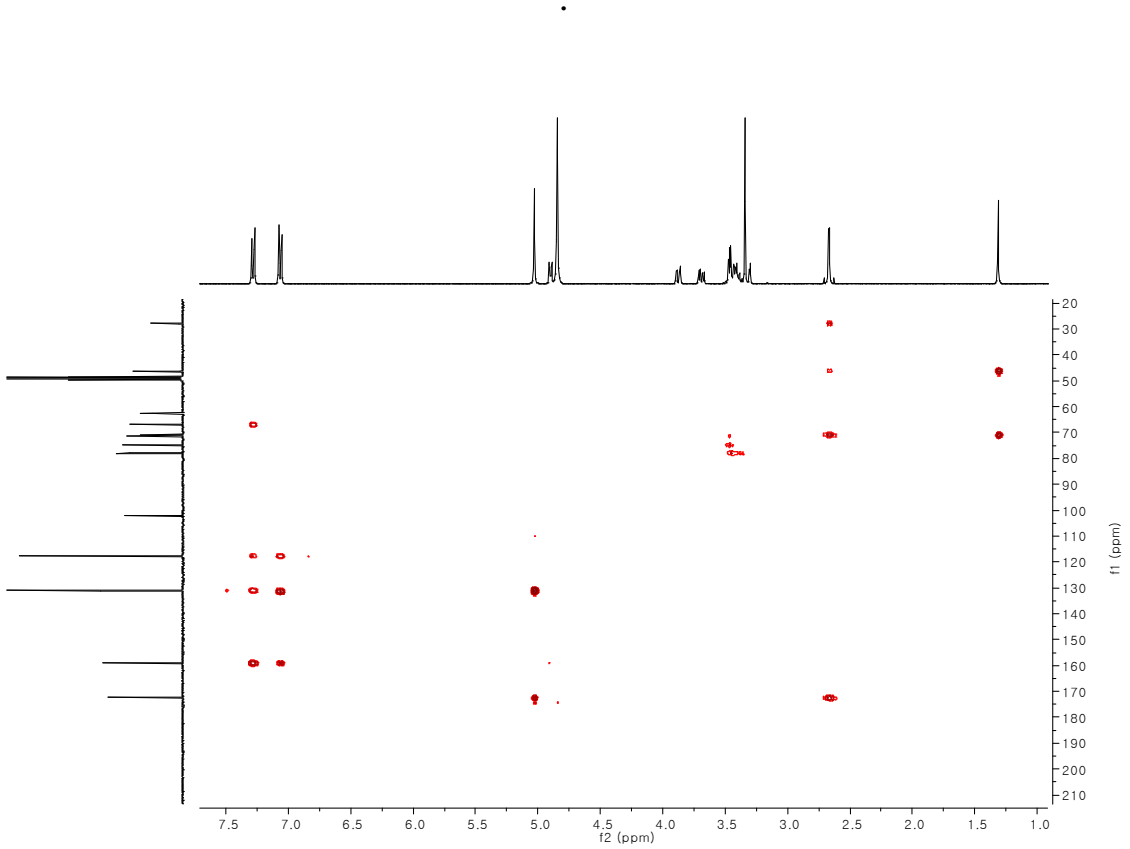

Figure 72. HMBC spectrum of compound **2** (400 MHz, CD_3OD)

국문초록

꾸지뽕나무 (*Cudrania tricuspidata*)는 뽕나무과 (Moreaceae)에 속하며, 낙엽소교목 또는 관목으로 한국, 일본 중국과 같은 동아시아에 분포한다. 꾸지뽕나무의 잎은 3개로 갈라지는 것과 난형인 것이 있으며, 꾸지뽕나무의 가지에는 가시가 있고, 가는 가지에는 털이 있다. 특히, 꾸지뽕나무의 뿌리와 열매의 경우, 화학 성분이 많이 분리 보고되어 왔지만 잎과 가지의 경우는 상대적으로 연구가 진행되지 않았다.

화합물의 분리를 위해 꾸지뽕나무의 잎과 가지를 100% 메탄올로 추출하여 감압 농축한 후, 추출물을 *n*-hexane, $CHCl_3$, EtOAc 그리고 *n*-BuOH 순으로 물과 함께 분획하였다. 각종 크로마토그래피 기법을 이용하여 EtOAC, *n*-BuOH 층에서 총 30개의 화합물을 분리하였으며, 화합물의 구조는 NMR, MASS 그리고 FT-IR spectroscopic data를 이용하여 동정하였다. 화합물은 4'-glucopyranosyloxybenzyl-4-*O*-*β*-D-glucopyranosyloxy-3,5-dimethoxybenzoate (**1**), Bis [4-*O*-*β*-D-glucopyranosyloxy)benzyl] 3-hydroxy-3-methylglutarate (**2**), Gastrodin (**3**), *p*-hydroxybenzaldehyde-4-*O*-*β*-D-glucopyranoside (**4**), 3,4,5-trimethoxy phenyl-1-*O*-*β*-D-glucopyranoside (**5**), Cudrabibenzyl A (**6**), (6*S*, 9*R*)-Roseoside (**7**), 3-*O*-caffeoyl-2-*C*-methyl-D-erythrono-1,4-lactone (**8**), Chlorogenic acid (**9**) Umbelliferone (**10**), Skimmin (**11**), Esculin (**12**), *C*-veratroylglycol (**13**), 2,3-dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)propan-1-one (**14**), 4-hydroxy benzoic acid (**15**), Methyl-4-hydroxy benzoate (**16**), Quercetin (**17**), Quercetin-3-*O*-*β*-D-glucopyranoside (**18**), Quercetin-7-*O*-*β*-D-glucopyranoside (**19**), Kaempferol-7-*O*-*β*-D-glucopyranoside

(**20**), Nicotiflorin (**21**), Aromadendrin (**22**), Aromadendrin-7-*O*-*β*-D-glucopyranoside (**23**), Gericudranin E (**24**), Taxifolin (**25**), Dihydromorin (**26**), Orobol (**27**), Orobol-7-*O*-*β*-D-glucopyranoside (**28**), Ambocin (**29**), 5-methoxy-8-glucopyranosyl-genistein (**30**)으로 동정하였으며, 화합물 **1-5**는 phenolic 계열, 화합물 **6**은 stilbenoid 계열, 화합물 **7**은 megastigmane 유도체, 화합물 **8-9**는 caffeoyl 유도체**,** 화합물 **10-12** 는 coumarin 계열, 화합물 **13-14**는 phenylpropanoid 계열, 화합물 **15-16**은 benzoic acid 유도체, 화합물 **17-30**은 flavonoid 계열 화합물이다. 이들 중, 화합물 **1**과 **2**는 천연에서 처음 분리 보고 되는 물질이며, 화합물 **3**, **4**, **5**, **13**, **14**, **15**, **16**, **29**는 뽕나무과에서 처음 발견되었으며, 화합물 **7**, **11**, **12**는 *Cudrania* 속에서 처음 발견된 물질이다.

주요어 : 꾸지뽕나무 (*Cudrania tricupidata*), 뽕나무과 (Moraceae), flavonoid

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